Adolf. von Baeyer.
Zur. freundlichen Erinnerung
an
W. H. Perkin jun
April 30th 1892.

Digitized by the Internet Archive
in 2007 with funding from
Microsoft Corporation

http://www.archive.org/details/researchinorgani02perkuoft

[Researches in organic Chemistry

by

William Henry Perkin

Vol. 2.

1889-1890]

350688
19.5.38

Contents

- On Berberin Part I.
- On Berberin Part II.
- Ethyl α α, diacetyladipate
- ω. ω diacetylbutane

The Synthetical Formation of Closed Carbon. C

- Part I (cont). The action of ethylene bromid the sodium compounds of ethylaceto and ethyl benzoylacetate.
- Part I (cont) The action of propylene bromid the sodium compounds of ethylacetoace and ethyl benzoylacetate.
- Part II (cont) Derivatives of Tetramethyle
- α. ω diacetylpentane and α. ω dibenzoylpen
- α. ω diacetyl α. ω. diethylpentane.
- Action of reducing agents on α α' diacetyl
Synthesis of dimethyl dihydroxy heptane ethy
- Action of dehydrating agents on α. α' diacetyl p
Synthesis of Methyl ethyl hexamethylene.
- Derivatives of Phenylhexamethylene
- Synthesis of Homologues of Pentane tetra-

- Action of Methylene iodide on the disodium compound of ethyl pentane tetracarboxylate. Synthesis of Hexamethylene derivatives.
- New synthesis of Hexamethylene dicarboxylic ac
- Synthesis of Hexahydro terephthalic acid.
- Acetylcarbinol.
- Acetopropylalcohol and Acetobutylalcoh
- Benzoylacetic acid and its derivatives. (Part
- Diphenyl furfuran.
- Note on the preparation of Pyrocatechol.
- Note on the formation of Anthraquinone f orthobenzoylbenzoic acid.

[*Reprinted from the Journal of the Chemical Society, February*, 1889. Vol. LV.]

350688
5 38
19

ON BERBERINE. (PART I.)

By W. H. PERKIN, Jun., Ph.D.

BERBERINE, the yellow alkaloïd of *Berberis vulgaris*, was discovered in the year 1826 by Chevallier and Pelletan (*Journ. de Chim. Médicale*, **2**, 314) in *Xanthoxylum clava Herculis*, and described by them under the name of xanthopicrit.

Subsequent researches have shown that this alkaloïd is a constituent of a large number of plants, in some of which it is present in considerable quantities.

It has been found in *Cocculus palmatus*, or Columbo root (Boedecker, *Annalen*, **66**, 384; **69**, 40); in *Berberis vulgaris* (Buchner, *Ann.*, **24**, 228); in *Cælœline polycarpa* (Stenhouse, *Ann.*, **95**, 108; **105**, 360); in the wood of *Coscinium fenestratum* from Ceylon, and in *Xanthorrisa apii folia*, a North American plant of the Ranunculacea order (Perrins, *Ann.*, **83**, 276); in *Hydrastis canadensis* (Mahla, *Sill. Am. J.* [2], **33**, 43 (1862)); another North American plant of the Ranunculacea order, which, as it contains about 4 per cent. of crude alkaloïd, and is readily obtainable in England, can be used as a source of the alkaloïd (Perrins, *Ann.*, Suppl. **2**, 173).

Berberine has also been found in *Woodumpar*, a yellow wood from Upper Assam, in the root of *Coptis tecta* or Mahmira—a plant growing in Hindoostan and China, and which is much valued in India on account of its tonic properties. Perrins (*loc. cit.*, p. 174), who examined this source, obtained as much as $8\frac{1}{2}$ per cent. berberine from the root—a far larger quantity than has up to the present been found in any plant.

The French chemists Chevallier and Pelletan, the discoverers of berberine, although they carefully and accurately described some of its properties, do not appear to have made any analyses of their

product, and it was not till 1835 that any attempts were made to ascertain the composition of this interesting substance. In this year, Buchner and Herberger (*Annalen*, **24**, 228) published the results of an important series of experiments on this alkaloïd, together with a number of analyses of the base itself, and also of its compound with oxide of silver. These experiments led them to the supposition that berberine was represented by the formula $C_{33}H_{36}N_2O_{12}$ (C = 6 : O = 8).

At a later date, Fleitmann made a careful examination of berberine, and showed that instead of being a weak acid, as Buchner had suggested, it was in reality a strong base, forming with acids stable salts, and in all respects showing the properties of a well-defined alkaloïd.

Fleitmann analysed not only berberine itself but also several of its salts, and the results of his experiments led him to the conclusion that the formula proposed by Buchner was erroneous, and that the composition of this base was $C_{42}H_{18}NO_9$ (C = 6 : O = 8).

In the year 1861, J. Dyson Perrins (*Annalen*, Suppl. **2**, 176) published the most accurate investigation of berberine which had up to that time been made, in the course of which he analysed a large number of its salts, and showed, in a most conclusive manner, that Fleitmann's formula was inaccurate, and that the true formula was $C_{20}H_{17}NO_4$ (C = 12 : O = 16).

Although the analytical results obtained by Perrins agree so closely with this formula, I still thought it necessary, before starting an investigation on the constitution of this interesting alkaloïd, to repeat some of these analyses with specially purified substances, so as to leave no doubt as to the relation of the carbon, hydrogen, nitrogen, and oxygen-atoms in it. The berberine used in these experiments was purified in the following manner :—

Crude berberine hydrochloride (from Merck in Darmstadt) was recrystallised twice from water acidified with hydrochloric acid, the beautiful yellow, silky needles dissolved in a little boiling water, and the solution rendered alkaline by the addition of an excess of carbonate of soda solution.

On cooling, the liquid became filled with brownish, silky crystals. These were filtered from the dark brownish-red mother-liquor, washed with water till the washings were only slightly yellowish, and dried on a porous plate. The beautiful silky mass thus obtained was next dissolved in boiling 80 per cent. alcohol (carefully purified methylated spirits may also be used) from which, on slowly cooling, long, yellowish-brown needles separated. After repeated crystallisation from dilute alcohol, these crystals entirely lose their original brownish colour, and are at length deposited in the form of long, silky needles of an intensely yellow colour. This substance was repeatedly analysed under varying conditions, but in spite of this no

satisfactory results could be obtained. One reason for this is that the substance contains several molecules of water of crystallisation, part of which is given off slowly at ordinary temperatures and part at 100°.

The substance dried at 100° is, however, never free from water of crystallisation, and if attempts are made to drive this off at a higher temperature, slight decomposition invariably takes place sufficient to spoil the analytical results. Another reason for the difficulty experienced in obtaining concordant numbers with berberine prepared in this way, is that the substance almost invariably contains traces of chlorine.

Experience showed that the nitrate, hydriodide, and platinochloride of berberine were far more suitable for analytical examination than the base itself.

Berberine Nitrate, $C_{20}H_{17}NO_4,HNO_3$.—This salt has been described by both Fleitmann and Perrins. It is readily prepared by adding an excess of dilute nitric acid to a warm, concentrated solution of the base. The nitrate is thus precipitated as a yellow crystalline mass, which is collected, well washed with water, and repeatedly recrystallised from this solvent. In this way beautiful yellow needles were obtained which, after drying first over sulphuric acid in a vacuum and then at 100°, gave the following results on analysis:—

I. 0·1724 gram substance gave 0·0722 gram H_2O and 0·3808 gram CO_2.

II. 0·1638 gram substance gave 0·0679 gram H_2O and 0·3621 gram CO_2.

III. 0·2056 gram substance gave 12·5 c.c. N. Bar = 760 mm. t = 15°.

	Theory. $C_{20}H_{17}NO_4,HNO_3$.		Found. I.	II.	III.	
C.....	60·30	p. c.	60·24	60·27	—	p. c.
H.....	4·52	,,	4·65	4·52	—	,,
N.....	7·04	,,	—	—	7·16	,,
O.....	28·14	,,	—	—	—	,,

These numbers agree well with those previously found by Fleitmann and Perrins, but not so well with those given by Henry.

	Fleitmann.			Perrins.		Henry.		
C....	60·15	59·64	p. c.	60·19	p. c.	59·09	59·44	p. c.
H...	4·75	4·62	,,	4·60	,,	4·85	4·84	,,

This salt is readily soluble in hot water, sparingly in cold, and almost insoluble in dilute nitric acid.

If the hot solution of berberine nitrate be mixed with a small quantity of ammonia, on cooling a remarkable compound separates in sparingly soluble golden plates. I have not as yet been able to determine the nature of this substance, but from the analyses already carried out it appears to have the formula $C_{20}H_{20}N_2O_9$.

(Found C = 55·2. H = 4·8. N = 6·80. Theory requires C = 55·55. H = 4·63. N = 6·48.)

I am at present engaged in the investigation of this substance.

Berberine Hydriodide, $C_{20}H_{17}NO_4,HI$.—This very insoluble salt is obtained as a yellow precipitate when an aqueous solution of berberine is acidified with a few drops of aqueous hydrogen iodide—or when potassic iodide is added to a solution of nitrate of berberine. The salt was collected, well washed with water, dried on a porous plate, and recrystallised from a large quantity of boiling 80 per cent. alcohol.

In this way, beautiful satiny needles were obtained which on analysis gave the following numbers:—

I. 0·1460 gram substance gave 0·0523 gram H_2O and 0·2767 gram CO_2.

II. 0·3561 gram substance gave 0·1795 gram AgI.

	Theory. $C_{20}H_{17}NO_4HI$.	Found. I.	Found. II.
C	51·83 p. c.	51·68	— p. c.
H	3·88 „	3·98	— „
I	27·43 „	—	27·25 „

Perrins and Henry, who also analysed this salt, obtained numbers agreeing closely with the above.

	Perrins.		Henry.
C	51·72	51·77 p. c.	51·59 p. c.
H	3·92	3·96 „	4·23 „
I	27·02	27·12 „	25·71 „

Berberine Platinochloride, $(C_{20}H_{17}NO_4)_2,H_2PtCl_6$.—This double salt has, on account of its insolubility and suitability for determining the molecular weight of berberine, been repeatedly examined. It is readily prepared by adding platinum chloride in excess to a slightly acid solution of berberine hydrochloride. The yellow precipitate thus thrown down was collected, well washed with water, dried on a porous plate over sulphuric acid, and then at 100°, and analysed with the following results:—

I. 0·2251 gram substance gave 0·0708 gram H_2O, 0·3657 gram CO_2, and 0·0406 gram Pt.

II. 0·6807 gram substance gave 0·1228 gram Pt.

III. 0·2780 gram substance gave 0·2192 gram AgCl.

	Theory. $(C_{20}H_{17}NO_4)_2H_2PtCl_6$.	Found. I.	II.	III	
C.....	44·47	p. c.	44·31	—	—	p. c.
H	3·33	„	3·49	—	—	„
Pt	18·02	„	18·03	18·08	—	„
Cl.....	19·73	„	—	—	19·50	„

Previous analyses of this salt by Fleitmann, Perrins, and Henry gave the following results, which are in each case the mean of a number of experiments :—

	Fleitmann.	Henry.	Perrins.
C	44·40 p. c.	44·38 p. c.	44·33 p. c.
H.....	3·50 „	3·57 „	3·41 „
Pt	18·11 „	17·90 „	18·21 „

This salt is almost insoluble in all the ordinary solvents. It crystallises from its solution in boiling amyl alcohol, on cooling in small, yellow needles, but it is extremely insoluble in this solvent even on boiling.

The analyses of these three salts show conclusively that the correct formula for berberine is $C_{20}H_{17}NO_4$. For a complete list of the various berberine salts which have from time to time been analysed by different investigators, I must refer to a paper by Hlasiwetz and Gilm (*Annalen*, Suppl. **2**, 197—201); and also to a recent paper by Ernst Schmidt (*Mittheilungen aus pharm. chem. Institut, Marburg*), which I have only lately had the opportunity of consulting.

In his researches on berberine (*loc. cit.*), Fleitmann states that it crystallises from water with $4\frac{1}{2}$ mols. H_2O. Several analyses which I made with different samples agree rather with the formula $C_{20}H_{17}NO_4 + 5\frac{1}{2}\ H_2O$. In these experiments the berberine used was prepared by Fleitmann's method, very carefully purified by repeated recrystallisation from water, and then dried in the air on a porous plate at the ordinary temperature. Determinations of the amount of water of crystallisation given off at 100° gave the following results :—

I. 1·5241 gram substance heated to 100° till constant lost 0·1944 gram.

II. 0·5883 gram substance heated to 100° till constant lost 0·0702 gram.

III. 0·6444 gram substance heated to 100° till constant lost 0·0758 gram.

IV. 0·7017 gram substance heated to 100° till constant lost 0·0851 gram.

Found.	I.	II.	III.	IV.
H_2O.....	12·7	11·9	11·9	12·1 p. c.

Complete analyses of different preparations of berberine dried at 100° till constant gave the following numbers:—

I. 0·2385 gram substance gave 0·1239 gram H_2O and 0·5550 gram CO_2.

II. 0·2095 gram substance gave 0·1041 gram H_2O and 0·4877 gram CO_2.

III. 0·1316 gram substance gave 0·0666 gram H_2O and 0·3032 gram CO_2.

IV. 0·3430 gram substance gave 11·4 c.c. N. $t = 16·5°$. Bar. = 736 mm.

	Theory.	Found.			
	$C_{20}H_{17}NO_4 + 2\frac{1}{2}H_2O$.	I.	II.	III.	IV.
C.....	63·16 p. c.	63·08	63·49	63·83	— p. c.
H	5·78 „	5·77	5·52	5·66	— „
N	3·68 „	—	—	—	3·72 „

From these analyses, it seems probable that berberine dried at 100° still contains $2\frac{1}{2}$ mols. H_2O, and that the air-dried substance originally contained $5\frac{1}{2}$ mols. H_2O, 3 of which are driven off at 100°. This would require a loss of 12·4 per cent., which agrees approximately with the numbers given above.

Hermann Schreiber (*Dissertation Marburg*, 1888) is of opinion that berberine crystallises with 6 mols. H_2O, all of which is expelled at 100° in a stream of hydrogen.

Properties of Berberine.

Berberine crystallises from water in brilliant, yellow needles, which when dried in the air have a fine silky lustre. The base itself and also its salts are remarkable for their excessively bitter taste; when warmed, they emit a faint but peculiar odour strongly resembling that of ordinary quinone.

When heated to 100°, the yellow berberine crystals gradually lose their lustre, and become yellowish-brown, at 110° the change is very

rapid, and at temperatures above 160° total decomposition soon sets in with formation of a brownish-black mass, from which I have not as yet been able to obtain anything of a crystalline nature.

On account of this behaviour of berberine when heated, I have not made any attempts to determine its melting point. Fleitmann (*loc. cit.*) gives as the melting point of berberine 120°, but this is certainly too low.

If bromine-water be added to even very dilute solutions of berberine, a yellow precipitate is produced, which on standing rapidly becomes darker. If the product is collected and washed with dilute sulphurous acid, a yellowish-orange mass is obtained, crystallising from large quantities of boiling water in needles, which appear to consist of the hydrobromide of a new base. Schreiber (*loc. cit.*, p. 38) considers this substance to be simply berberine hydrobromide.

Berberine not only combines with acids to form salts, but it also gives peculiar compounds with alkalis. The addition of methyl alcoholic potash to a strong solution of berberine in alcoholic potash produces a pinkish-white, amorphous precipitate, which contains considerable quantities of inorganic matter. The analyses of this compound have not as yet given satisfactory results.

Berberine does not appear to combine either with hydroxylamine or phenylhydrazine, and although the alkaloïd dissolves readily in a mixture of oxychloride and pentachloride of phosphorus, no change seems to take place even when the mixture is allowed to remain for a long time at ordinary temperatures.

Before publishing the details of the experiments which have been made in this direction, I propose to confirm the results already obtained, by using, instead of the alkaloïd itself, some salt, such as the nitrate, which contains no water of crystallisation.

In its behaviour towards reagents, berberine shows the following characteristic reactions:—

It dissolves in concentrated sulphuric acid, forming a yellow solution, which on warming turns olive-green.

Very dilute solutions of berberine give with chlorine-water a decided brownish-red coloration, whilst strong solutions are coloured intensely by this reagent. Reducing agents, such as tin and hydrochloric acid, destroy this colour, which, however, reappears on the further addition of chlorine-water.

Concentrated nitric acid dissolves berberine, forming a dark, reddish-brown solution, from which water precipitates a yellow, flocculent mass, partly soluble in ammonia. If the brown-red solution in nitric acid be warmed, oxidation rapidly sets in with evolution of abundance of red fumes, and formation of a yellow solution which contains ber-

beronic acid, oxalic acid, and other products. Potassium ferricyanide in alkaline solution gives with berberine a yellow precipitate, being itself for the most part reduced to ferrocyanide.

If a trace of berberine be boiled for a short time with concentrated aqueous hydrogen iodide, the product diluted with water and rendered slightly alkaline by the addition of ammonia, an intense blackish-violet coloration is produced.

Berberine is also characterised by the insolubility of some of its compounds, as, for instance, its hydriodide, platinochloride, aurochloride, chromate, &c., whilst a number of soluble salts, such as the nitrate, are rendered almost insoluble by the addition of a mineral acid.

A solution of iodine in potassic iodide gives with extremely small quantities of berberine salts a brownish precipitate of the periodide, $C_{20}H_{17}NO_4,HI,I_2$. If the precipitation be carefully conducted in warm alcoholic solution, beautiful, shining, green plates separate.

Berberine Hydrochloride, $C_{20}H_{17}NO_4,HCl + 2H_2O$.—This beautiful salt crystallises from water in long, yellow needles. As mentioned at the commencement of the paper, this salt, in spite of its beautiful appearance, does not give very satisfactory results on analysis.

If attempts are made to dry it at 100°, in a short time the yellow colour of the crystals gradually changes to brownish-yellow, and then to brownish-red, small quantities of hydrochloric acid being invariably lost during the operation. Analysis of the pure substance dried over sulphuric acid gave numbers agreeing fairly well with those required by the formula $C_{20}H_{17}NO_4,HCl + 2H_2O$.

I. 0·2075 gram substance gave 0·1057 gram H_2O and 0·4461 gram CO_2.

II. 0·1557 gram substance gave 0·0792 gram H_2O and 0·3383 gram CO_2.

III. 0·5091 gram substance gave 16·5 c.c. N. Temp. = 17°. Bar. 727 mm.

	Theory.	Found.			
	$C_{20}H_{17}NO_4.HCl + 2H_2O$.	I.	II.	III.	
C	58·89 p. c.	58·63	59·25	—	p. c.
H	5·39 „	5·66	5·65	—	„
N	3·43 „	—	—	3·63	„

The difficulty in obtaining good results in the analysis of this substance is partly accounted for by the fact that the salt dried as above is so excessively hygroscopic as to render it very difficult to weigh it out with the necessary degree of accuracy.

As the result of a number of careful analyses, E. Schmidt (*loc. cit.*,

p. 54) has shown that berberine hydrochloride crystallises from dilute alcohol with 4 mols. H_2O.

Oxidation of Berberine with Potassium Permanganate.

In most of the investigations on the constitution of the alkaloïds which have up to the present time been carried out, it has been found that the careful examination of the behaviour of this class of substances towards oxidising agents has almost invariably given interesting results, and in some cases very important clues as to their structure.

The molecule of the alkaloïd is usually split up, yielding acids of much simpler constitution, such as hemipinic acid (from narcotine), carboxylic acids of pyridine, quinoline, and their derivatives (in the case of quinine, cinchonine, &c.), &c., although in some cases acids containing nearly the same number of carbon-atoms as the alkaloïd employed are obtained.

One of the most remarkable examples of the value of careful oxidation in investigating an alkaloïd is that of papaverine, from which by the use of potassium permanganate under various conditions Goldschmiedt was able to obtain among other substances papaverinic, veratric, hemipinic, pyridinetricarboxylic, and dimethyloxycinchoninic acids and papaveraldine.

Experiments on the oxidation of berberine with potassic permanganate have already been made by E. Schmidt and C. Schilbach (*Arch. Pharm.* [3], **25**, 164—170; Abstr., 1887, 604), who obtained thus considerable quantities of hemipinic acid.

In some preliminary experiments on berberine made early in 1887, I also obtained hemipinic acid in considerable quantities by the oxidation of berberine with alkaline permanganate, and lately, in view of the remarkable results obtained by Goldschmiedt in his examination of hemipinic and isohemipinic acids (*Monats.*, 1888, 861), I have again very carefully studied this decomposition, partly with the object of determining whether the acid obtained is simply hemipinic acid or a mixture of this acid with metahemipinic acid, and partly from a desire to obtain some substance intermediate between berberine and this acid, which might afford some clue to the constitution of the alkaloïd.

The first experiments were carried out almost exactly in the way Goldschmiedt recommends in his first paper on papaverine (*Monats.*, 1885, 1112).

30 grams of pure berberine hydrochloride were dissolved in 1 litre of boiling water, the salt decomposed by the addition of 6 grams of potassic carbonate, and then oxidised by slowly running

in 150 grams of potassic permanganate dissolved in 3 litres of hot water. At first the oxidation is very rapid, but as soon as about two-thirds of the permanganate have been added, decolorisation takes place much more slowly, continued boiling being necessary to remove the last traces of the oxidiser.

At the end of this operation, the product was saturated with carbonic acid, filtered through a cloth filter, and the manganese precipitate well pressed; this was then carefully extracted by repeated boiling with water, and pressing in a vice. The filtrate and washings were evaporated to dryness, the residue pulverised and repeatedly exhausted with boiling absolute alcohol (or purified methylated spirits), the alcoholic solution distilled, and the residue, after freeing it from the last traces of alcohol by gently warming on a water-bath, was dissolved in a little water and filtered. On acidifying with dilute sulphuric acid, the brown aqueous solution deposits a small quantity of a resinous precipitate, from which, however, nothing crystalline could be obtained. It was removed by filtration, the clear filtrate extracted 20 times with pure ether, the ethereal solution dried over calcic chloride and evaporated, and the brownish residue thus obtained was allowed to remain for some days over sulphuric acid in a vacuum. The crude semi-solid mass was then roughly purified by spreading it on a porous plate, and afterwards repeatedly recrystallised from boiling water. In this way beautiful transparent crystals were obtained, which on analysis gave numbers agreeing with those required for hemipinic acid :—

0·1827 gram substance gave 0·0720 gram H_2O and 0·3550 gram CO_2.

	Theory. $C_{10}H_{10}O_6$.	Found.
C	53·10 per cent.	52·99 per cent.
H	4·42 „	4·38 „
O	42·48 „	42·73 „

Determination of water of crystallisation :—

0·8878 gram of substance heated to 100° till constant lost 0·1236 gram = 13·92 per cent. Theory for $C_{10}H_{10}O_6 + H_2O$ = 13·74 per cent.

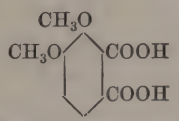
Considerable difference of opinion exists as to the melting point of hemipinic acid. Wegscheider (*Monats.*, **3**, 351) gives 175—179° for the acid from narcotine; Liebermann (*Ber.*, **19**, 2279), 180—181°, and Grüne (*Ber.*, **19**, 230) 180°, whereas E. Schmidt and Schilbach (*Arch. Pharm.*, **225**, 164) found for the hemipinic acid prepared by them from berberine, and also for the acid from narcotine, the low melting point 160—161°. Goldschmiedt, who has lately most

carefully re-examined the hemipinic acid from narcotine, found that although when rapidly heated it melted at 172—175° with decomposition into anhydride and water, yet when slowly heated it melted at 160—161°. I have repeated these experiments with the hemipinic acid from berberine, and although I can corroborate the experience of Goldschmiedt that the melting point varies considerably according to the rapidity of the heating, still I have never been able to observe a melting point lower than 170°. When heated moderately rapidly, the acid obtained as above melts regularly at 177—178° with decomposition.

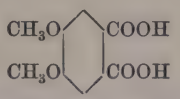
In studying the action of small quantities of permanganate on berberine, I subsequently obtained an acid, $C_{10}H_{10}O_6$, of totally different appearance, which melted at 159—160° with decomposition, and thus showed all the properties of hemipinic acid from narcotine.

As I was, therefore, not quite satisfied that the acid obtained as described above, melting at 177—178°, was hemipinic acid and not metahemipinic acid, I carefully examined my product in the way suggested by Goldschmiedt (*Monats.*, 1888, 870).

In his researches on papaverine, Goldschmiedt obtained by the oxidation with alkaline permanganate an acid of the formula $C_{10}H_{10}O_6$, which from its properties (m. p. 174—175°, water of crystallisation, &c.) he at first supposed to be identical with the hemipinic acid from narcotine. The further study of the constitution of papaverine, however, showed that these two acids could not be identical, but must be isomeric merely, a conclusion which was borne out by the further examination of their properties. As both these acids on fusion with potash give protocatechuic acid, and both are orthocarboxylic acids, their constitution must be represented by the formulæ—



Hemipinic acid from narcotine.



Metahemipinic acid from papaverine.

In examining the hemipinic acid from berberine, I first made a determination of the methoxyl-groups according to Zeisel's method (decomposition with hydrogen iodide and determination of the amount of methyl iodide formed by leading into an alcoholic solution of silver nitrate, and estimating the silver iodide precipitated (*Monats.*, 1883, 704), with the following results:—

0·2740 gram substance dried at 100° gave 0·7350 gram AgI.

	Found.	Theory for $C_{10}H_{10}O_6$.
OCH_3....	27·74 per cent.	27·43 per cent.

In order, then, to prove that the acid from berberine was a derivative of pyrocatechol, a small quantity was decomposed by fusion with potash. 2 grams of the pure acid was dissolved in a little potash, the solution evaporated to dryness, and the residue fused in a silver dish with 50 grams of pure caustic potash and a little water for about half an hour. The resulting almost colourless melt was dissolved in water and acidified with dilute sulphuric acid, during which operation the solution became first blue, then violet, and lastly reddish, but remained clear. It was extracted several times with ether, the ethereal solution dried over calcic chloride, and the ether distilled off; in this way, a crystalline residue was obtained which, after recrystallising once or twice from a little water, gave the following results on analysis:—

0·1217 gram substance dried at 100° gave 0·0442 gram H_2O and 0·2436 gram CO_2.

	Theory. $C_7H_6O_4$.	Found.
C	54·55 per cent.	54·59 per cent.
H	3·89 ,,	4·03 ,,
O	4·56 ,,	4·48 ,,

A determination of the water of crystallisation gave the following results:—

0·3326 gram of air-dry substance dried at 100° lost 0·0347 gram.

	Theory. $C_7H_6O_4 + H_2O$.	Found.
H_2O	10·46 per cent.	10·43 per cent.

This acid has, therefore, the composition of protocatechuic acid, with which it agrees in all its properties.

It crystallised from hot water in needles melting at 195—196°. The aqueous solution gives with ferric chloride a deep, emerald-green coloration, which, on the careful addition of sodic carbonate solution, becomes first blue, then violet, and at last red. It reduces an ammoniacal silver solution at once, gives with lead acetate a white precipitate soluble in acetic acid, and on heating is decomposed into carbonic anhydride and a white crystalline sublimate which shows all the reactions of pyrocatechol. These reactions, however, do not determine whether the acid obtained from berberine is hemipinic or metahemipinic acid, as both these acids contain two methoxyl-groups, and

both on fusion with potash yield protocatechuic acid. These two acids can, however, be readily distinguished by conversion into their ethylimides; the ethylimide of hemipinic acid melting at 96°, whilst that of metahemipinic acid melts at 226—227°.

In order to prepare the ethylimide of the acid from berberine, the pure substance was dissolved in an aqueous solution of ethylamine, the solution evaporated to dryness on a water-bath, and the residue distilled from a small retort. The solid distillate was dissolved in a little boiling methyl alcohol and allowed to stand, when beautiful needle-shaped crystals were obtained, which on analysis gave the following numbers:—

0·1753 gram substance gave 9·7 c.c. N. Bar. = 760 mm. t = 14·5°.

	Theory. $C_{12}H_{13}NO_4$.	Found.
N.....	5·96 per cent.	6·09 per cent.

This ethylimide melts at 94—95°, but when recrystallised from water, at 96°, and shows all the properties of ethylhemipinimide, prepared by Liebermann by the action of ethyl iodide on the potassium-derivative of hemipinimide. It is therefore proved beyond doubt that hemipinic acid from berberine is identical with that obtained from narcotine.*

Besides hemipinic acid, there are small quantities of at least two other acids formed when berberine is oxidised with permanganate in the proportions given above, both of which are present in the potassic carbonate residues, from which the potash salt of hemipinic acid has been extracted with alcohol. These residues were dissolved in a small quantity of water, neutralised with acetic acid, and treated with acetate of copper. On long standing in a warm place, the green solution thus produced deposited a small quantity of a light bluish-green precipitate. This was collected, well washed with water, and decomposed by passing sulphuretted hydrogen through the salt suspended in boiling water; the filtrate, on evaporation, gave a small quantity of a crystalline residue which on examination was found to contain nitrogen.

On recrystallising from water, small nodular crystals were obtained, melting at 238—242°. These gave on analysis the following numbers:—

0·2629 gram substance gave 14·5 c.c. N. Bar = 759. t = 14°.

	Theory. $C_8H_5NO_6 + H_2O$.	Found.
N	6·11 per cent.	6·48 per cent.

* This confirms the results obtained by E. Schmidt (*loc. cit.*, 63—73).

Unfortunately the amount of this acid obtained by this reaction was too small to allow of further experiments being made to determine its composition, but from its melting point and analysis it would appear to be either carbocinchomeronic acid or berberonic acid. This is the more probable, as berberine when oxidised by nitric acid yields berberonic acid. It is interesting to notice that E. Smith and C. Schilbach (*Arch. Pharm.* [3], **25**, 164—170) in their experiments on the oxidation of berberine with permanganate, also noticed the formation of a nitrogenous acid, crystallising in nodular crystals, and melting at 218—220°. The silver salt, however, gave numbers showing this acid to be a pyridinemonocarboxylic acid (nicotinic acid?).

The mother-liquor from the copper salt was treated with sulphuretted hydrogen, filtered from the precipitated sulphide of copper, and subacetate of lead added so long as a precipitate was produced. The lead salt was collected, well washed, suspended in water, decomposed with sulphuretted hydrogen, and the filtered solution evaporated to dryness.

The residue, when dissolved in a small quantity of boiling water, and the solution allowed to cool slowly, deposited, after some time, a quantity of crystals; these, on examination, were found to consist of two distinct substances, the one crystallising in thick, brownish prisms, and the other in long, colourless needles. The brownish prisms were mechanically separated, recrystallised several times from water, and the colourless crystalline mass thus obtained dried at 100°, and analysed with the following result:—

0·1932 gram substance gave 0·0777 gram H_2O and 0·3763 gram CO_2.

	Theory $C_{10}H_{10}O_6$.	Found.
C	53·10 per cent.	53·12 per cent.
H	4·42 „	4·47 „
O	42·48 „	42·41 „

As this substance melted at 177—178°, there can be no doubt that it was simply hemipinic acid, with which it agreed in all its reactions.

The needle-shaped crystals obtained from the lead salt together with the hemipinic acid, after recrystallisation from water, were found to consist of pure oxalic acid. It is very remarkable that in the oxidation of berberine with alkaline permanganate so little oxalic should be formed. The amount actually obtained from 60 grams of berberine was but little more than 3 grams.

From the above it will be seen that berberine, when oxidised with an excess of potassium permanganate, yields principally hemipinic

acid, the other oxidation products isolated being formed only in very small quantity. In this respect, berberine differs very widely from papaverine, which, under similar conditions, yields a number of important decomposition products, such as papaverinic acid, $C_{16}H_{13}NO_7$, veratrinic acid, $C_9H_{10}O_4$, metahemipinic acid, $C_{10}H_{10}O_6$, α-pyridine-tricarboxylic acid, $C_8H_5NO_6$, &c., all of which are found in considerable quantity in the product of the oxidation. The reason for this is that berberine and its derivatives are so very readily oxidised, that unless a limited amount of permanganate is used, and the oxidation very carefully carried out, the whole molecule is split up, yielding principally hemipinic acid. As the result of a very large number of experiments carried out under a great variety of conditions, it has, however, been found possible to arrest the oxidation before it has gone as far as hemipinic acid, and in this way several new substances have been isolated, the study of which it is hoped will furnish some important clue as to the constitution of this interesting alkaloïd.

In experimenting on the formation of these new derivatives I have found it necessary to work with small quantities at a time (never more than 7 grams of berberine in one operation), as when large quantities are used, even under precisely similar conditions of temperature and amount of oxidiser, very small yields are obtained.

The best results have been obtained with the following quantities:—

5 grams berberine (dried at the ordinary temperature).
9 „ potassic permanganate.
$1\frac{1}{2}$ „ „ carbonate.

The potassic permanganate and carbonate are dissolved in half a litre of water of 90°, and the solution very slowly run through a separating funnel or burette, into a hot solution (90°) of the berberine (in a quarter of a litre of water), the whole being well stirred during the operation. As soon as all the permanganate has been added (the oxidation requires about 10—15 minutes), the product is transferred to a flask, cooled well under the tap, and the manganese precipitate brought into solution by passing a slow stream of sulphurous acid into the mixture. In this way a slightly yellowish liquid is obtained, in which are suspended small, yellow, flocculent particles. These are collected, well washed with water, and freed from the last traces of mother-liquor by spreading them on a porous plate. The purification of the resulting amorphous yellow mass which contains at least three new substances, is a very difficult operation, and has, up to the present, only been successfully carried out when the following conditions have been carefully observed.

The well washed residue is suspended in water and well agitated

at a temperature of about 40°, with a slight excess of sodic carbonate, by which treatment the crude product is separated into two portions, the one soluble, the other insoluble in carbonate of soda; these are separated by filtration.

The new acid contained in the brownish-coloured filtrate is deposited on the addition of an acid in the form of an amorphous yellow precipitate, which, on account of the presence of a quantity of a resinous substance, can only with difficulty be obtained in a crystalline condition. The method of purification which has given the best results is the following:—The solution in sodic carbonate is nearly neutralised with dilute sulphuric acid, and the new acid fractionally precipitated in three fractions by running into the well-stirred solution a fine stream of very dilute sulphuric acid. The first fraction should be about one-fourth, the second one-half, the third one-fourth of the whole. The second fraction is carefully washed, dried on a porous plate, dissolved in a little methyl alcohol, and the solution transferred to a flat dish, and allowed to evaporate completely at the ordinary temperature. During the evaporation, the new acid separates in yellow nodular masses, covered with a transparent resin, which is invariably deposited along with the crystals. The resulting mixture of acid and resin is scraped off the sides of the dish and well kneaded between the fingers with a small quantity of methyl alcohol. In this way the resin is removed, leaving the warty masses almost entirely undissolved. The purified product is now dissolved in a small quantity of boiling methyl alcohol, from which it is deposited on cooling in almost colourless nodular masses, which, after repeated recrystallisation, gave the following results on analysis:—

I. 0·1511 gram substance gave 0·0602 gram H_2O and 0·3192 gram CO_2.

II. 0·1421 gram substance gave 0·0552 gram H_2O and 0·3000 gram CO_2.

III. 0·3633 gram substance gave 10·4 c.c. N. $t = 11°$. Bar. = 727 mm.

	Theory.			Found.			
	$C_{20}H_{17}NO_9$.	$C_{20}H_{19}NO_9$.		I.	II.	III.	
C	57·83	57·55	per cent.	57·61	57·58	—	per cent.
H	4·10	4·55	„	4·43	4·47	—	„
N	3·37	3·36	„	—	—	3·40	„
O	34·70	34·53	„	—	—	—	„

It is as yet very difficult to decide whether this new substance has the formula $C_{20}H_{17}NO_9$ or $C_{20}H_{19}NO_9$, but for various reasons I am

inclined, in the meantime, to adopt the latter formula, leaving the definite settlement of this point to further experimental proof.

This substance is readily soluble in ethyl and methyl alcohol and in acetic acid, but only sparingly in benzene, toluene, and ether, and almost insoluble in light petroleum, chloroform, ethyl acetate, and cold water. It is, however, best purified by recrystallisation from methyl alcohol, from which it is deposited, on long standing, either in warty masses or in small plates.

Considerable difficulty was experienced in determining the melting point of this new substance. When rapidly heated, it softens at about 138—140°, and then melts completely at 141—142° with evolution of gas. At 150—155° it again becomes solid, and on further heating melts again between 195° and 200°.

The pure compound, $C_{20}H_{19}NO_9$, dissolves readily in alkalis and in alkaline carbonates.

The barium salt was prepared by dissolving the acid in baryta-water, removing the excess of the latter by passing carbonic anhydride through the boiling solution, filtering, and evaporating on a water-bath. In this way a quantity of an almost colourless crystalline barium salt was obtained which, after washing with a little water and drying first over sulphuric acid in a vacuum and then at 100°, gave the following results on analysis :—

0·4598 gram substance gave 0·1926 gram $BaSO_4$.

Theory. $C_{20}H_{17}NO_9Ba$.		Found.	
Ba ..	24·82 per cent.	Ba ..	24·63 per cent.

The neutral solution of the ammonium salt of this acid gives with *nitrate of silver* a white, gelatinous precipitate, soluble in a large quantity of boiling water: with *cupric acetate* a beautiful bluish-green precipitate, and, with *acetate of lead*, a white, gelatinous precipitate. Fused with a small quantity of pure caustic potash, this substance is readily decomposed, yielding an almost colourless melt which, when dissolved in water, acidified with sulphuric acid, and extracted with ether, gives a crystalline acid readily soluble in water. The solution of this acid gives with ferric chloride a deep-green coloration, changing to violet and then to deep red on the addition of sodic carbonate. As it also gives with acetate of lead a white precipitate, and readily reduces ammoniacal silver solution, it is probable that this substance is either berberinic acid or protocatechuic acid.

The residual product of the oxidation of berberine, insoluble in sodic carbonate, obtained as described above, contains, besides a quantity of a resinous substance, two new compounds which are separated in the following way :—

The crude, brownish product is well washed, first with a dilute solution of sodic carbonate, then several times with water, dried on a porous plate, and dissolved in a small quantity of boiling 90 per cent. acetic acid (5 grams of substance require about 20 grams of acetic acid). This solution on cooling gradually deposits a considerable quantity of a crystalline substance. At the end of 48 hours, this is collected, washed with a little glacial acetic acid, and purified by repeated recrystallisation from this solvent.* It is thus obtained in flat, glittering plates, with a remarkable silky lustre: these after drying, first on a porous plate and then at 100°, gave the following results on analysis:—

I. 0·2001 gram substance gave 0·0800 gram H_2O and 0·4387 gram CO_2.

II. 0·1395 gram substance gave 0·0569 gram H_2O and 0·3053 gram CO_2.

III. 0·1354 gram substance gave 0·0550 gram H_2O and 0·2971 gram CO_2.

IV. 0·1560 gram substance gave 0·0620 gram H_2O and 0·3433 gram CO_2.

V. 0·3773 gram substance gave 11·2 c.c. N ($t = 13°$. Bar. = 760 mm.).

VI. 0·3372 gram substance gave 10·6 c.c. N ($t = 13·5°$. Bar. = 737 mm.).

	Theory. $C_{20}H_{17}NO_3$.	Found. I.	II.	III.	IV.	V.	VI.	
C	60·15 p. c.	59·87	59·69	59·77	60·02	—	—	p. c.
H	4·26 „	4·44	4·53	4·51	4·41	—	—	„
N	3·51 „	—	—	—	—	3·50	3·58	„
O	32·08 „	—	—	—	—	—	—	„

This substance melts at 236—237°. It is readily soluble in hot acetic acid, from which it crystallises on cooling in beautiful glittering plates, but is only sparingly soluble in ethyl and methyl alcohol, benzene, toluene, light petroleum, and acetone, even on boiling. Although insoluble in alkaline carbonates, this substance dissolves readily in warm solutions of ammonia, caustic potash, &c., forming well-defined salts. If the solution in ammonia be allowed to evaporate over sulphuric acid, a very curious jelly-like ammonium salt is deposited, which gradually dries up to a mass resembling dried albumin. This dissolves readily in water, and the solution gives with reagents some very characteristic salts.

* The mother-liquors contain considerable quantities of a second neutral substance, which will be described further on.

Nitrate of silver gives a white, gelatinous precipitate which is readily soluble in hot water, but only sparingly in cold; it could not be recrystallised, as it somewhat readily decomposes on warming with water. A small quantity of this salt was prepared, well washed with cold water, dried on a piece of porous plate over sulphuric acid in a vacuum, and analysed with the following results :—

I. 0·1996 gram substance gave 0·0560 gram H_2O, 0·2547 gram CO_2, and 0·0623 gram Ag.

II. 0·3286 gram substance gave 0·1023 gram Ag.

	Theory: $C_{20}H_{15}NO_8Ag_2 + 4H_2O$.	Found. I.	Found. II.
C	35·04 p. c.	34·80	— p. c.
H	3·35 „	3·12	— „
Ag	31·40 „	31·22	32·13 „

From this analysis it would appear as though the neutral substance, $C_{20}H_{17}NO_8$, when dissolved in alkalis took up 4 mols. H_2O, forming a bibasic acid of the formula $C_{20}H_{25}NO_{12}$. It is, however, much more probable that the silver salt when prepared as above contains water of crystallisation, as is the case, for example, with the silver salt of papaverinic acid, which crystallises with 2—$2\frac{1}{2}$ mols. H_2O. The formula of the acid formed by dissolving the substance $C_{20}H_{17}NO_8$ in alkalis, can therefore only be accurately determined by the analysis of some other of its salts, with the investigation of which I am at present engaged.

The solution of the ammonium salt of this acid gives with *acetate of copper* a splendid, light bluish-green precipitate, and with *acetate of lead* a white, gelatinous precipitate which dissolves somewhat sparingly in boiling water. The chlorides of *barium* and *calcium* give no precipitate in the cold; on boiling, white, amorphous salts are precipitated.

The mother-liquors from the precipitation of the substance $C_{20}H_{17}NO_8$ contain, besides small traces of this sparingly soluble substance, a considerable quantity of a second neutral substance which is much more readily soluble. To isolate this, the dark-brown acetic acid solution is heated to boiling, diluted with one-fourth of its bulk of boiling water, and allowed to stand for 24 hours. The crystals which separate are collected, the mother-liquor again treated as above, and the operation repeated until no more crystals separate. In this way nearly the whole of the new substance crystallises out in yellowish plates, whereas if too much water be added at first the crystals are invariably mixed with a black, tarry substance which hinders their subsequent purification. The crude substance thus obtained can now

easily be purified by recrystallisation, once from dilute acetic acid and twice from pure alcohol. From the hot, alcoholic solution it is deposited on cooling in beautiful colourless plates with a pearly lustre. For analysis the substance was dried at 100°.

I. 0·1372 gram substance gave 0·0540 gram H_2O and 0·3155 gram CO_2.

II. 0·1792 gram substance gave 0·0741 gram H_2O and 0·4093 gram CO_2.

III. 0·1395 gram substance gave 0·0584 gram H_2O and 0·3213 gram CO_2.

IV. 0·1680 gram substance gave 0·0720 gram H_2O and 0·3852 gram CO_2.

V. 0·3070 gram substance gave 10·1 c.c. N ($t = 15°$. Bar. = 742 mm.).

VI. 0·2493 gram substance gave 8·2 c.c. N ($t = 18·5°$. Bar. = 759 mm.).

	Theory. $C_{20}H_{17}NO_7$.	Found. I.	II.	III.	IV.	V.	VI.	
C	62·66 p. c.	62·71	62·61	62·81	62·53	—	—	p. c.
H	4·43 „	4·38	4·70	4·65	4·76	—	—	„
N	3·66 „	—	—	—	—	3·75	3·80	„
O	29·24 „	—	—	—	—	—	—	

This new compound, which from the analysis appears to have the formula $C_{20}H_{17}NO_7$, melts at 150°. It is readily soluble in hot methyl and ethyl alcohol, but only sparingly soluble in these liquids in the cold. It dissolves with difficulty in boiling water, and the solution on slowly cooling deposits the substance in beautiful, glittering plates, which resemble anthracene in appearance; if rapidly cooled, however, the aqueous solution becomes milky before crystallising. It is also readily soluble in hot, but almost insoluble in cold benzene and toluene. If this substance is not quite pure, its solutions fluoresce in a most beautiful way, reminding one strongly of a dilute solution of fluoresceïn.

The substance $C_{20}H_{17}NO_7$ does not dissolve in alkalis in the cold, and only very slowly on boiling. The solution in hot, strong caustic potash on cooling deposits what appears to be the unchanged substance, but as the substance is more soluble in caustic potash than in water, it is possible that it forms with alkalis very unstable salts. Fused with a little potash, the substance $C_{20}H_{17}NO_7$ yields what appears to be protocatechuic acid (? berberinic acid). In studying this decomposition, about $\frac{1}{4}$ of a gram of substance was gently fused with 2 grams of potash and a little water in a thick test-tube. The crystals dissolved at once with evolution of quantities of a pungent

gas, which resembled methylamine or ethylamine rather than ammonia. The colourless residue dissolved in water with a reddish colour, and on acidifying and extracting with ether, a colourless crystalline substance was obtained, which showed all the properties of protocatechuic acid. The aqueous solution gave with ferric chloride a deep-green coloration, which on the addition of sodic carbonate became first blue, then violet, and at last red. On the addition of acetate of lead to the aqueous solution, a white precipitate was obtained, soluble in acetic acid.

The substance $C_{20}H_{17}NO_7$ dissolves in strong nitric acid with a deep orange colour, and in warm sulphuric acid forming a deep violet-black solution. The addition of strong hydrochloric acid causes the crystals to turn yellow without dissolving them, and if a drop of hydrochloric acid be added to the alcoholic solution of the substance the solution is coloured slightly yellow, and acquires a bluish-green fluorescence.

In order to further control the formula of the substance $C_{20}H_{17}NO_7$, its molecular weight was determined by Raoult's method, with the following result:—

Substance taken	0·7558 gram.
Acetic acid	42·1296 „
Melting point of acetic acid.....	16·447°
„ of mixture.....	16·263
Depression of melting point.....	0·184

Molecular weight of substance found from the above data	380
Theory for $C_{20}H_{17}NO_7$	383

The yield of crude, dry, yellow substance obtained by the oxidation of 200 grams of berberine as described above is about 70 grams, of which 12 grams are insoluble, and 55 grams soluble in a solution of sodic carbonate. These numbers show clearly that a large portion of the products of the oxidation must be contained in the filtrate from the yellow substance. In order to test this, the yellow solution was evaporated over a free flame, with occasional addition of a little aqueous sulphurous acid, until the inorganic salts commenced to separate as a crust on the surface. The liquid was then allowed to cool, filtered from the crystalline matter, and again evaporated, the operation being repeated until the solution from the oxidation of 200 grams of berberine was reduced in bulk to 1 litre. The brownish product was then extracted 20 times with ether, the ethereal solution dried over calcic chloride, and the ether distilled off until about 150 c.c. remained.

During this operation a quantity of a white, crystalline substance separates, which after collecting, washing with a little ether, and

drying on a porous plate, presented the appearance of hard, sandy crystals. Subsequent examination showed that this product was a mixture of two substances, which are readily separated from each other by recrystallisation from water. The solution in a small quantity of boiling water deposits on cooling first of all a quantity of glittering plates, which are rapidly filtered off. On standing, the second substance separates from the mother-liquor in hard prisms.

The more insoluble substance, which is formed only in very small quantity, was purified by recrystallisation from water; the crystals, dried first over sulphuric acid in a vacuum and then at 100°, gave the following numbers on analysis:—

I. 0·1493 gram substance gave 0·0618 gram H_2O.

II. 0·2907 „ „ 8·8 c.c. N; $t = 17°$. Bar. = 757 mm.

	Theory. $C_{20}H_{19}O_9$.	Found.
C.....	57·55 per cent.	57·54 per cent.
H.....	4·55 „	4·60 „
N.....	3·35 „	3·50 „
O.....	34·53 „	34·36 „

This interesting substance, which from the above analysis appears to have the constitution $C_{20}H_{19}NO_9$, melts at 178—179° with decomposition, due probably to loss of water. It is sparingly soluble in alcohol and ether, fairly soluble in boiling water, from which it crystallises on cooling, either in small plates, or in very small, warty masses.

At present only sufficient of this substance has been obtained for the above analyses, and subsequent investigation must show whether the constitution assigned to it is correct.

This acid has the same formula as the acid obtained from the yellow precipitate (p. 78), but as it melts 38° higher it must be isomeric, and not identical with this substance.

The crude crystals of the more soluble substance obtained, as described above, were separated from the substance $C_{20}H_{17}NO_9$ by repeated recrystallisation from water, from which they were invariably deposited as a hard, crystalline crust on the bottom of the beaker. The air-dried crystals, when heated on a water-bath, lost scarcely any weight, showing the absence of water of crystallisation.

On analysis the following numbers were obtained:—

I. 0·1518 gram substance gave 0·0608 gram H_2O and 0·2970 gram CO_2.

II. 0·1720 gram substance gave 0·0701 gram H_2O and 0·3361 gram CO_2.

	Theory. $C_{10}H_{10}O_6$.	Found. I.	Found. II.
C	53·10 p. c.	53·36	53·28 p. c.
H	4·42 „	4·45	4·52 „
O	42·48 „	42·19	42·20 „

This substance melts at 159—160° with decomposition, and as it gives protocatechuic acid on fusion with potash, there can scarcely be a doubt that it is hemipinic acid. It is, however, in appearance totally different from the hemipinic acid previously obtained (see p. 73). The crystals, which contain no water of crystallisation, are very soluble in hot water, and separate from the solution very slowly indeed, the deposition often being incomplete after standing for 24 hours.

The hemipinic acid obtained as described at the commencement of this chapter, and also a sample of the same substance prepared from narcotine (for which I am indebted to Dr. Goldschmiedt), crystallise rapidly with 2 mols. H_2O of crystallisation, when the hot aqueous solution is allowed to cool moderately slowly. The crystals dried at 100°, and heated under the same conditions as the above, melt at 177—178° with decomposition.

The great difference in the properties of the two preparations lead me to doubt their identity, and in order to establish this the silver salt of the acid, melting at 159—160°, was prepared and examined. This salt is thrown down on the addition of silver nitrate to the ammonium salt as a heavy, white precipitate. It was well washed with water, dried over sulphuric acid in a vacuum, and then analysed with the following result:—

I. 0·2928 gram substance gave 0·1430 gram Ag.
II. 0·2505 „ „ 0·1222 „

	Theory. $C_{10}H_8O_6Ag_2$.	Found. I.	Found. II.
Ag	49·09 p. c.	48·83	48·78 p. c.

This salt gives therefore the same numbers as those required for the silver salt of hemipinic acid.

Subsequent experiments on these two preparations of hemipinic acid make it appear probable that this substance exists in two distinct forms, the one melting at 159—160°, and the other at 177—178°. If a crystal of the latter acid be added to a warm saturated solution of the former, in some cases at least, the one modification is completely converted into the other, but this change appears only to take place under certain conditions of concentration, &c.

I hope to be able to investigate this point more completely at an early date.

Action of Hydrogen Iodide on Berberine.

When heated with fuming aqueous hydrogen iodide, berberine is readily decomposed with evolution of methyl iodide, and formation of a new substance, which dissolves in alkalis with a blackish-violet coloration. This preliminary experiment led me to suppose that berberine is decomposed by hydrogen iodide in a way similar to papaverine, which under this treatment is split up into papaveroline, $C_{16}H_{13}NO_4$, and 4 mols. of methyl iodide. In determining the constitution of berberine, it was a matter of great importance to discover the number of OCH_3 groups contained in the formula $C_{20}H_{17}NO_4$, and this is readily done by Zeisel's method (*Monats.*, **6**, 995), which consists in decomposing the alkaloïd with fuming hydrogen iodide, and determining the amount of methyl iodide formed by means of alcoholic silver nitrate. The first experiments in this direction were made with berberine itself, with the following results:—

I. 0·2930 gram of berberine (dried at 100—110°) gave 0·3990 gram AgI.

II. 0·3315 gram of berberine (dried at 100—110°) gave 0·4440 gram AgI.

III. 0·3290 gram of berberine (dried at 100—110°) gave 0·4430 gram AgI.

	Theory for $2(OCH_3)$ groups in $C_{20}H_{17}NO_4 + H_2O$.	Found.		
		I.	II.	III.
(OCH_3)	17·56 p. c.	18·03	17·72	17·83 p. c.

These experiments show that berberine contains only two OCH_3 groups in its molecule, these two being present in the portion which on oxidation yields hemipinic acid. Owing, however, to the difficulty in determining accurately the amount of water of crystallisation present in the samples of berberine used, these results were not considered perfectly trustworthy, and in order to be quite certain similar experiments were instituted with the nitrate and hydriodide of the base, these salts being so readily obtained pure and free from water of crystallisation.

I. 0·3903 gram berberine nitrate, dried at 100°, gave 0·4669 gram AgI.

	Theory for $2(OCH_3)$ groups in $C_{20}H_{17}NO_4,HNO_3$.	Found.
(OCH_3)	15·59 per cent.	15·74 per cent.

II. 0·4401 gram berberine hydriodide gave 0·4520 gram AgI.

	Theory for $2(OCH_3)$ groups in $C_{20}H_{17}NO_4,HI$.	Found.
(OCH_3)	13·39 per cent.	13·61 per cent.

In order, if possible, to isolate the phenolic substance formed during this reaction, the experiment was carried out with larger quantities. 25 grams of pure berberine were boiled with a considerable excess of fuming aqueous hydrogen iodide in a flask connected with a reflux condenser, until evolution of methyl iodide had ceased.

The dark-coloured solution on cooling deposited a small quantity of the new substance in the form of blackish-coloured nodules. These were collected, the solution distilled from a small retort until half had passed over and again allowed to cool, when a further quantity of solid was obtained. The crude product was well washed with water till free from hydrogen iodide, and ground to a paste in a mortar with a weak solution of sulphurous acid, to remove a small quantity of iodine. The yellowish-brown emulsion was now collected on a filter-pump, well washed with water, and extracted with boiling water containing a little sulphurous and sulphuric acids. The hot solution, after filtering from a quantity of a brown insoluble residue, deposited the new substance on cooling in beautiful orange-coloured, amorphous flocks, which entirely filled the liquid. These were collected, reprecipitated twice from hot water containing sulphurous acid, dried over sulphuric acid in a vacuum, and analysed, with the following result:—

I. 0·1478 gram substance gave 0·0582 gram H_2O and 0·3097 gram CO_2.

II. 0·1546 gram substance gave 0·0631 gram H_2O and 0·3244 gram CO_2.

III. 0·4354 gram substance gave 15·2 c.c. N; $t = 0·12$. Bar. = 740 mm.

IV. 0·4086 gram, decomposed by nitric acid according to Carius' method, gave 0·1314 gram $BaSO_4$.

V. 0·4401 gram, decomposed by nitric acid according to Carius' method, gave 0·1412 gram $BaSO_4$.

I*a*. 0·2784 gram substance, heated to 100° till constant, lost 0·0123 gram.

II*a*. 0·2502 gram substance, heated to 100° till constant, lost 0·0112 gram.

	Theory.	Found.					
	$(C_{18}H_{13}NO_4)_2,H_2SO_4 + 2H_2O$.	I.	II.	III.	IV.	V.	
C.....	57·75 p. c.	57·12	57·22	—	—	—	p. c.
H.....	4·28 „	4·37	4·60	—	—	—	„
N.....	3·74 „	—	—	4·01	—	—	„
H_2SO_4..	13·10 „	—	—	—	13·52	13·45	„
H_2O....	4·81 „	4·43	4·47	—	—	—	„

This substance is therefore the sulphate of a base of the formula $C_{18}H_{13}NO_4$, for which I propose the name *berberoline*.

This base is formed from berberine simply by substituting hydrogen for methyl in each of the two methoxy-groups; thus:—

$C_{18}H_{11}NO_2(OCH_3)_2$. Berberine. $C_{18}H_{11}NO_2(OH)_2$. Berberoline.

The sulphate of this base is stable, and does not appear to undergo decomposition even on long standing. In the presence of a trace of alkali, decomposition sets in at once owing no doubt to oxidation—a dark, blackish-violet solution being formed. An aqueous solution of the sulphate shows the following reactions:—

Chlorine-water gives a dark-violet, flocculent precipitate. *Nitric acid* gives a magnificent violet coloration which on standing—and particularly on warming—becomes a deep, reddish-brown. Berberoline solutions decompose solutions of platinic chloride, auric chloride, and ammoniacal nitrate of silver with separation of the metal.

Fusion of Berberine with Potash.

Hlasiwetz and Gilm (*Jahresbericht*, 1864, 407), who were the first to study the action of melted potash on berberine, obtained by this decomposition two new substances, that is, berberinic acid, $C_8H_8O_4 + H_2O$, and an acid of the formula $C_9H_8O_5$. With the object of determining the constitution of these two acids, I have again taken up the study of this important decomposition, the experiment being conducted as follows:—

100 grams of caustic potash and 5 c.c. of water were heated in a silver dish to about 180° and then 60 grams of berberine slowly added in small portions at a time. The berberine on coming in contact with the melted potash was rapidly decomposed—little black balls being formed at first, which swam about on the surface of the liquid, but on stirring, as the temperature gradually rose (to 240°), these dissolved, forming a dark-brown liquid. During the operation—which lasts about an hour—a quantity of thick vapours, smelling strongly of ammonia and guaiacol, were evolved. The pro-

duct was dissolved in water, acidified with dilute sulphuric acid, filtered from a quantity of brownish flocks which separated, evaporated to a syrupy consistence, and well agitated with about twice its volume of strong alcohol. The potassic sulphate thus precipitated was filtered off, washed with a little alcohol, the combined alcoholic solutions gently evaporated on a water-bath, and the residue, dissolved in a little water, was repeatedly extracted with ether. The ethereal extract after carefully drying over calcic chloride and evaporating deposited 5 grams of a dark-brownish, crystalline mass consisting of impure berberinic acid. This was purified first by spreading it on a porous plate and then by repeated recrystallisation from water. The beautiful white crystals thus obtained gave on analysis the following numbers :—

I. 0·1506 gram substance dried at 80° gave 0·0667 gram H_2O and 0·3160 gram CO_2.

II. 0·1683 gram substance dried at 80° gave 0·0735 gram H_2O and 0·3521 gram CO_2.

	Theory. $C_8H_8O_4$.	Found. I.	Found. II.
C	57·15 p. c.	57·22	57·05 p. c.
H	4·76 ,,	4·92	4·84 ,,
O	38·04 ,,	37·86	38·11 ,,

Berberinic acid appears to crystallise with 1 mol. H_2O, which, however, is gradually given off at the ordinary temperatures if the crystals are placed over sulphuric acid in a vacuum. The melting point of this acid, which is not given by Hlasiwetz and Gilm, I found to be about 165°. No accurate melting point can be given, as when heated the substance softens at 145°, and then melts with evolution of carbonic anhydride at about 165° ; this temperature may therefore be looked upon as its decomposing point rather than its melting point.

The other properties of this acid agree in all respects with those given by Hlasiwetz and Gilm.

If a drop of ferric chloride is added to an aqueous solution of berberinic acid, a splendid dark-green coloration is produced which, on the addition of sodic carbonate solution, becomes first violet, then violet-red, and at last deep-red coloured. This reaction, and the fact that this acid reduces Fehling's solution and an ammoniacal solution of silver nitrate, and gives with acetate of lead a white precipitate soluble in acetic acid, shows at once that berberinic acid must be very closely related to protocatechuic acid.

As protocatechuic acid on distillation is split up into pyrocatechol and carbonic acid, it was thought that, under similar treatment,

berberinic acid might give some decomposition-product which would afford some clue as to its constitution. In order to test this, 2 grams of the pure dry acid were heated in a small retort until the evolution of carbonic anhydride had ceased, and the residue then rapidly distilled. In this way an almost colourless syrup was obtained, which on analysis gave the following numbers:—

0·1460 gram substance gave 0·0842 gram H_2O and 0·3605 gram CO_2.

	Theory. $C_7H_8O_2$.	Found.
C	67·74 per cent.	67·37 per cent.
H	6·46 „	6·41 „
O	25·80 „	26·22 „

This substance has, therefore, the same formula as homopyrocatechol, with which it agrees in all its reactions. It is readily soluble in water; the solution reduces Fehling's solution and ammoniacal nitrate of silver. Ferric chloride produces a deep-green coloration which, on the addition of sodic carbonate, becomes reddish-violet. There can, therefore, be no doubt that berberinic acid on distillation is split up into homopyrocatechuic and carbonic acid, thus:—

$$C_8H_8O_4 = C_7H_8O_4 + CO_2,$$

but it is at present difficult to decide the positions of the carboxyl-group with reference to the OH and CH_3-groups.

I am at present engaged on the further investigation of oxidising agents on berberine and on the alkyl addition-products of tetrahydroberberine, and also on a series of experiments on the constitution of berberonic acid.

The completion of these experiments will be somewhat delayed owing to an unfortunate fire in the laboratories of the Heriot Watt College having consumed a number of new products which had already been prepared. For this reason also I have not been able to complete the examination of the substances described in this paper so thoroughly as I could have wished.

I hope, however, at an early date to be able to communicate to the Society a further paper on this interesting alkaloïd.

Heriot Watt College,
Chemical Laboratory, Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

ON BERBERINE.

PART II.

[*Reprinted from the Journal of the Chemical Society, Dec.*, 1890. Vol. LVII.].

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

On Berberine. Part II.*

By W. H. Perkin, Jun., Ph.D., F.R.S.

CONTENTS.

PAGE

Introduction 993
Constitution of Anhydroberberilic and Berberilic Acids 998
Examination and Constitution of Berberal 1000
Constitution of Berberine 1003

Oxidation of Berberine with Potassium Permanganate ..... 1010.

Table showing the Separation of the Substances obtained by the Oxidation of Berberine 1014

ω-Amidoethylpiperonylcarboxylic Anhydride, $C_{10}H_9NO_3$ 1013
1. Acetylamidoethylpiperonylcarboxylic Anhydride, $C_{12}H_{11}NO_4$ 1016
2. Amidoethylbromopiperonylcarboxylic Anhydride, $C_{10}H_8BrNO_3$ 1017
3. Nitrosoamidoethylpiperonylcarboxylic Anhydride, $C_{10}H_8N_2O_4$ 1018
4. Hydroxyethylpiperonylcarboxylic Acid, $C_{10}H_{10}O_5$, and its Anhydride, $C_{10}H_8O_4$ 1020
5. Hydroxyethylbromopiperonylcarboxylic Acid, $C_{10}H_9BrO_5$, and its Anhydride, $C_{10}H_7BrO_4$ 1025
6. Hydroxyethylnitropiperonylcarboxylic Anhydride, $C_{10}H_7N_2O_6$ 1027
7. Hydroxyethylcatecholcarboxylic Anhydride, $C_9H_8O_4$ 1027
8. Action of Phosphorus Pentachloride on the Anhydride $C_{10}H_8O_4$; Chlorethylpiperonylcarboxylic Acid, $C_{10}H_9ClO_4$ 1029
9. Methylic Chlorethylpiperonylcarboxylate, $C_{11}H_{11}ClO_4$ 1032
10. Oxyhydrastinine, $C_{11}H_{11}NO_3$ 1034
11. Ethylamidoethylpiperonylcarboxylic Anhydride, $C_{12}H_{13}NO_3$ 1035
12. Phenylamidoethylpiperonylcarboxylic Anhydride, $C_{16}H_{13}NO_3$ 1036

Anhydroberberilic Acid, $C_{20}H_{17}NO_8$, *and its Salts* 1037
1. Methyl Salt of Anhydroberberilic Acid, $C_{21}H_{19}NO_8$ 1039
2. Acetylanhydroberberilic Acid, $C_{22}H_{19}NO_9$ 1041
3. Anhydroberberilic Chloride, $C_{20}H_{16}NClO_7$ 1042
4. Amide of Anhydroberberilic Acid, $C_{20}H_{18}N_2O_7$ 1046
5. Anilide of Anhydroberberilic Acid, $C_{26}H_{22}N_2O_7$ 1047

Berberilic Acid, $C_{20}H_{19}NO_9$, *and its Salts* 1048
1. Dimethyl Salt of Berberilic Acid, $C_{22}H_{23}NO_9$ 1050
2. Action of Heat on Berberilic Acid 1051
3. Hydrolysis of Berberilic Acid: Preparation of ω-Amidoethylpiperonylcarboxylic Acid, $C_{10}H_{11}NO_4$ 1053

* Part I, Trans., 1889, 63.

PAGE
4. Dibenzoylamidoethylpiperonylcarboxylic Acid, $C_{24}H_{19}NO_6$ 1059
5. Action of Nitrous Acid on Amidoethylpiperonylcarboxylic Acid. Formation of Hydroxyethylpiperonylcarboxylic Acid 1060

Synthesis of Anhydroberberilic Acid..... 1061

Berberal, $C_{20}H_{17}NO_7$..... 1062
1. Hydrolysis of Berberal. Preparation of Pseudopianic Acid, $C_{10}H_{10}O_5$ 1064
2. Action of Potassium Hydrate on Pseudopianic Acid. Formation of Veratric Acid, $C_9H_{10}O_4$..... 1067
3. Oxime of Pseudopianic Acid, $C_{10}H_{11}NO_5$ 1069
4. Action of Heat on the Oxime of Pseudopianic Acid. Formation of Hemipinimide, $C_{10}H_9NO_4$..... 1070
5. Oxime of Opianic Acid, $C_{10}H_{11}NO_5$ 1070
6. Reduction of Pseudopianic Acid. Formation of Pseudomeconine, $C_{10}H_{10}O_4$ 1072
7. Pseudomeconinic Acid, $C_{10}H_{12}O_5$ 1073
8. Action of Alkalis on Berberal. Formation of Pseudopianic Acid, $C_{10}H_{10}O_5$; Pseudopianate of Amidoethylpiperonylcarboxylic Anhydride, $C_{20}H_{19}NO_8$, and of Amidoethylpiperonylcarboxylic Anhydride, $C_{10}H_9NO_3$..... 1075
9. Action of Phenylhydrazine on Berberal 1077
10. Synthesis of Berberal..... 1079
11. Pseudopianate of Amidoethylpiperonylcarboxylic Anhydride, $C_{20}H_{19}NO_8$..... 1080

Isoberberal, $C_{20}H_{17}NO_7$..... 1081
Opianate of ω-Amidoethylpiperonylcarboxylic Anhydride, $C_{20}H_{19}NO_8$... 1082

Separation of Oxyberberine, Dioxyberberine, and Anhydroberberilic Acid ... 1083
Oxyberberine, $C_{20}H_{17}NO_5$..... 1085
Dioxyberberine, $C_{20}H_{17}NO_6$ 1087
Action of Alkalis on Dioxyberberine..... 1089
Berilic Acid, $C_{20}H_{15}NO_8$ 1091
Hemipinic Anhydride, $C_{10}H_8O_5$ 1094
Hydrastic Acid, $C_9H_6O_6$ 1095
Berberine Hydrogen Sulphite, $C_{20}H_{17}NO_4,H_2SO_3$..... 1097
Examination of the Mother Liquors of Berberilic Acid and of Berberal.. 1098
Examination of the Aqueous Mother Liquors from the Oxidation of Berberine..... 1105

Introduction.

In a paper communicated to the Society some time since, I showed that berberine, $C_{20}H_{17}NO_4$, when very carefully oxidised with potassium permanganate in alkaline solution, yields, besides hemipinic acid and other simply constituted substances, a number of interesting derivatives, containing the same number of carbon atoms as the alkaloïd itself.

The further study of the oxidation of berberine has led to the isolation of some new compounds still containing 20 carbon atoms, and

the exhaustive examination of these has given many results which afford a very clear insight into the constitution of the alkaloïd.

The most important of these derivatives are the following:—

Oxyberberine	$C_{20}H_{17}NO_5$,
Dioxyberberine.....	$C_{20}H_{17}NO_6$,
Berberal	$C_{20}H_{17}NO_7$,
Anhydroberberilic acid.....	$C_{20}H_{17}NO_8$,
Berberilic acid	$C_{20}H_{19}NO_9$.

and these, with the exception of the last-named, are derived from berberine by the addition of 1, 2, 3, and 4 oxygen atoms.

Before explaining in detail the methods employed in preparing and separating these compounds, I propose to give a short sketch of the results of the experiments which have thrown the most light on the constitution of berberine. In doing this it will be well to commence with anhydroberberilic acid, as the study of the properties of this substance served as a foundation on which the examination of the other derivatives was based. Anhydroberberilic acid is almost insoluble in aqueous alkalis and alkaline carbonates at ordinary temperatures, but when warmed with dilute sodium hydrate solution it is readily dissolved, yielding a salt of *berberilic acid*:—

$$C_{20}H_{17}NO_8 + 2NaOH = C_{20}H_{17}NO_9Na_2 + H_2O.$$

As the free acid, at temperatures above 170°, is reconverted into anhydroberberilic acid, it was at first supposed that berberilic acid was a bibasic acid, containing two carboxyl groups in the ortho-position, and that anhydroberberilic acid was simply its anhydride; subsequent examination showed, however, that although the latter compound is undoubtedly an anhydride of berberilic acid, it is at the same time itself an acid and not a neutral compound.

In support of this statement the following facts may be mentioned:—

1. Under certain conditions (explained in detail in the experimental part of this paper) anhydroberberilic acid forms salts of the formula $C_{20}H_{16}NO_8M'$.
2. When treated with phosphorus pentachloride, anhydroberberilic is converted into the corresponding acid chloride $C_{20}H_{16}NClO_7$, thus:—

$$C_{20}H_{17}NO_8 + PCl_5 = C_{20}H_{16}NClO_7 + POCl_3 + HCl.$$

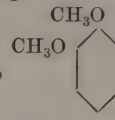
From this chloride, the amide $C_{20}H_{16}N(NH_2)O_7$ and the anilide $C_{20}H_{16}N(NH{\cdot}C_6H_5)O_7$ have been prepared.

An insight into the constitution of anhydroberberilic acid was

first obtained by the study of berberilic acid, $C_{20}H_{19}NO_9$. This acid is readily obtained by dissolving the anhydro-acid in warm dilute alkalis, and precipitating the alkaline solution with dilute hydrochloric acid; it is a bibasic acid forming salts of the formula $C_{20}H_{17}NO_9M'_2$.

The most interesting salt of this acid is the ammonium salt, $C_{20}H_{17}NO_9(NH_4)_2$, as this when gently warmed or allowed to stand over sulphuric acid in a vacuum, gradually loses half its ammonia, yielding the ammonium salt of anhydroberberilic acid:—

$$C_{20}H_{17}NO_9(NH_4)_2 = C_{20}H_{16}NO_8(NH_4) + H_2O + NH_3.$$

Although only slowly acted on by alkalis, berberilic acid dissolves readily in boiling dilute sulphuric acid, being at the same time decomposed quantitatively into hemipinic acid,  , and a new base, $C_{10}H_{11}NO_4$, thus:—

$$C_{20}H_{19}NO_9 + H_2O = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COOH\\COOH\end{matrix} + C_{10}H_{11}NO_4.$$

When heated at 180° or digested with strong aqueous potassium hydrate, or even when simply boiled with water for some time, this base loses the elements of a molecule of water, and is converted into its inner anhydride, $C_{10}H_9NO_3$, thus:—

$$C_{10}H_{11}NO_4 = C_{10}H_9NO_3 + H_2O.$$

This important substance is feebly basic, its salts being only stable in the presence of large quantities of acid. By the action of nitrous acid, it is converted into a yellow nitroso-compound, $C_{10}H_8(NO)NO_3$, which, when boiled with dilute caustic soda, rapidly dissolves with evolution of nitrogen, thus:—

$$C_{10}H_8(NO)NO_3 + H_2O = C_{10}H_{10}O_5 + N_2.$$

This substance, $C_{10}H_{10}O_5$, is a monobasic acid, the salts of which are fairly characteristic. When heated to 150° or boiled with water, it readily loses 1 mol. of water and is converted into its inner anhydride, $C_{10}H_8O_4$, thus:—

$$C_{10}H_{10}O_5 = C_{10}H_8O_4 + H_2O.$$

This anhydride is reconverted by dissolution in alkalis into the acid $C_{10}H_{10}O_5$.

Numerous experiments were tried with the object of oxidising this substance to some well known acid, but without success, the compound being either unacted on or else completely destroyed by the

oxidising agents employed. When gently fused with potash, the substance yields a mixture of catechol and protocatechuic acid. This reaction affords some clue to the constitution of this series of compounds, as it proves them to be derivatives of orthodihydroxybenzene; as, however, on the other hand, these substances give no reaction with ferric chloride, the absence of hydroxyl groups must be assumed.

When the anhydride $C_{10}H_8O_4$ was heated with hydriodic acid in Zeisel's apparatus (*Monatsh.*, **6**, 995), not a trace of methyl iodide was evolved, proving the absence of methoxy-groups; decomposition had, however, evidently taken place, as ether extracted from the residue in the retort a dark coloured substance which gave an intense green coloration with ferric chloride, but could not be obtained in a crystalline condition.

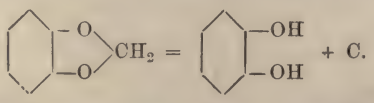
Hydrochloric acid at 170—175° decomposes the compound $C_{10}H_8O_4$, apparently quantitatively, with deposition of carbon and formation of a new compound, $C_9H_8O_4$, thus:—

$$C_{10}H_8O_4 = C_9H_8O_4 + C.$$

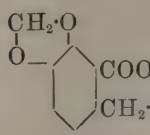
This, with ferric chloride, gives the most intense catechol reaction; it also gives a white precipitate with acetate of lead, and reduces both Fehling's solution and ammoniacal nitrate of silver. This decomposition into carbon and a catechol derivative on heating with water or dilute hydrochloric acid is characteristic of piperonyl derivatives* (Fittig, Remsen, *Annalen*, **159**, 139), and the above experiment, therefore, proves that the derivatives obtained from the base $C_{10}H_{11}NO_4$ (including the base itself) must contain the piperonyl group, $CH_2<^{O}_{O}>C_6H_4$.

As also, the fact that the two compounds $C_{10}H_{11}NO_4$ and $C_{10}H_{10}O_5$ are readily converted into inner anhydrides proves that they, and therefore their derivatives, must contain two side chains in the ortho-position, the following formulæ may be taken as representing the constitution of these derivatives.

* The nature of this reaction may perhaps be rendered more clear by the partial equation—



For the sake of brevity, I propose that the group $C_6H_4<^{O}_{O}>CH_2$, which occurs in such a large class of compounds, shall be simply called "*piperonyl*."

$C_{10}H_{11}NO_4$ =  = ω-Amidoethylpiperonylcarboxylic acid.*

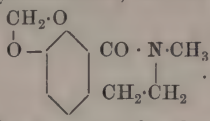
$C_{10}H_9NO_3$ = $CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot NH\\CH_2\cdot CH_2\end{matrix}$ = ω-Amidoethylpiperonylcarboxylic anhydride.

$C_{10}H_8(NO)NO_3$ = $CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot N(NO)\\CH_2\cdot CH_2\end{matrix}$ = Nitroso-ω-amidoethylpiperonylcarboxylic anhydride.

$C_{10}H_{10}O_5$ = $CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2\cdot O\end{matrix}$ = ω-Hydroxyethylpiperonylcarboxylic acid.

$C_{10}H_8O_4$ = $CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix}$ = ω-Hydroxyethylpiperonylcarboxylic anhydride.

$C_9H_8O_4$ = $\begin{matrix}HO\\HO\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix}$ = ω-Hydroxyethylcatecholcarboxylic anhydride.

Freund and Will (*Berichte*, **20**, 2400), in their researches on hydrastine, describe a substance, oxyhydrastinine, obtained by the action of caustic potash on hydrastinine, which they subsequently prove to have the constitution  .

If the formulæ assigned to the compounds above be correct, oxyhydrastinine must be a methyl derivative of the compound $C_{10}H_9NO_3$, and in order to confirm these formulæ every effort was made to convert the substance $C_{10}H_9NO_3$ into oxyhydrastinine.

This proved to be extremely difficult, and numerous experiments, extending over several months, failed to bring about the desired result. The transformation was, however, ultimately accomplished in the following way:—

The compound $C_{10}H_8O_4$, when heated with phosphorus pentachloride, is converted into the chloride of ω-chlorethylpiperonylcarboxylic acid, thus:—

$$C_{10}H_8O_4 + PCl_5 = C_{10}H_8O_3Cl_2 + POCl_3,$$

* The relative portion of the two pairs of ortho-side chains is very probably that given here, but further experiments are needed before this view can be definitely accepted.

which, when decomposed by water, is converted into the acid $C_{10}H_9O_4Cl$, thus:—

$$C_{10}H_8O_3Cl_2 + H_2O = C_{10}H_9O_4Cl + HCl.$$

This new acid is remarkable for the ease with which it loses hydrogen chloride, and is converted into the compound $C_{10}H_8O_4$, thus:—

$$C_{10}H_9O_4Cl = C_{10}H_8O_4 + HCl.$$

This change takes place on heating at 150°, or on warming with alkalis or reducing with zinc-dust and acetic acid, and also on heating with methylamine in alcoholic solution in a sealed tube. In order to prevent this, the carboxyl group was protected by converting the chloro-acid into its methyl salt, $C_{10}H_8(CH_3)O_4Cl$. This methyl salt, when heated with methylamine in alcohol solution at 130° for six hours, and the product boiled with alcoholic potash, is almost quantitatively converted into oxyhydrastinine, thus:—

$$CH_2{<}{}^{O}_{O}{>}C_6H_2{<}{}^{COOCH_3}_{CH_2\cdot CH_2Cl} + 2NH_2\cdot CH_3 =$$

$$CH_3\cdot NH_2,HCl + CH_2{<}{}^{O}_{O}{>}C_6H_2{<}{}^{COOCH_3}_{CH_2\cdot CH_2\cdot NH\cdot CH_3} =$$

$$CH_2{<}{}^{O}_{O}{>}C_6H_2{<}{}^{CO\cdot NCH_3}_{CH_2\cdot CH_2} + CH_3\cdot OH.$$

Oxyhydrastinine.

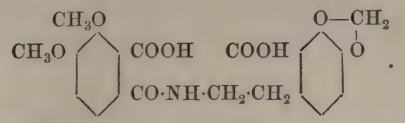
The substance thus obtained melts at 98°, and is identical with oxyhydrastinine, and the synthesis of this compound from ω-amidoethylpiperonylcarboxylic acid affords conclusive proof that the constitutional formulæ given above to this substance and its derivatives are correct.

An examination of these formulæ shows also that berberine is an isoquinoline and not a quinoline derivative, and the decomposition of berberilic acid into hempinic acid and ω-amidoethylpiperonylcarboxylic acid affords evidence that this alkaloïd must be closely related to papaverine, hydrastine, and narcotine (p. 1004).

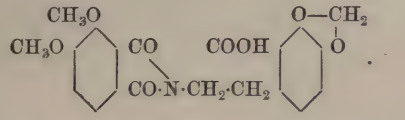
As berberine is an isoquinoline derivative, the statement of Bernheimer (*Gazzetta*, **13**, 342) that berberine, when fused with potash, yields quinoline cannot be correct; it is probable that the substance which he obtained was isoquinoline.

Constitution of Berberilic Acid and Anhydroberberilic Acid.

As berberilic acid is a bibasic acid, and as, on hydrolysis, it yields hempinic acid and ω-amidoethylpiperonylcarboxylic acid, its constitution must be represented by the formula



Anhydroberberilic acid is a monobasic acid, and is derived from berberilic acid by the elimination of one molecule of water; its formula is therefore



Additional proof of the correctness of these formulæ is afforded by the synthesis of anhydroberberilic acid.

This interesting synthesis is readily accomplished by heating the hemipinate of *ω*-amidoethylpiperonylcarboxylic acid, which is formed by evaporating mixed aqueous solutions of hempinic and *ω*-amidoethylpiperonylcarboxylic acids. This reaction is readily understood with the aid of the following equations:—

$$\begin{aligned}&(CH_3O)_2C_6H_2\langle{}^{COOH}_{COO\cdot NH_3\cdot CH_2\cdot CH_2}\rangle C_6H_2\langle{}^{COOH}_{O}{}^{O}\rangle CH_2 =\\ &\qquad (CH_3O)_2C_6H_2\langle{}^{CO}_{CO\cdot N\cdot CH_2\cdot CH_2}\rangle C_6H_2\langle{}^{COOH}_{O}{}^{O}\rangle CH_2 + 2H_2O.\end{aligned}$$

In Part I of this research (*loc. cit.*, pp. 78 and 84) two substances are described which have the same formula as berberilic acid.

One of these compounds melts at 140—141°, and is very closely related to berberilic acid, because, when heated to 180°, it, like berberilic acid, is quantitatively converted into anhydroberberilic acid; as, however, berberilic acid melts at about 180°, it would seem that the two acids are isomeric and not identical.

The melting point of berberilic acid is, however, lowered to an unusually marked degree by the least trace of impurity, and it is therefore necessary that further experimental data should be forthcoming, before the isomerism of the two acids can be considered as proved. It is, nevertheless, interesting to note that, theoretically, two substances of the formula $C_{20}H_{19}NO_9$ are possible, both of which on heating would be converted into the same anhydroberberilic acid; and there seems to be no reason why, by slightly altering the conditions of formation or hydrolysis, the acid isomeric with berberilic acid might not be formed.

The constitution of one of these isomeric acids would be represented by the formula given above for berberilic acid; the second acid would have the constitution represented by the formula

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\text{—}\\COOH\end{matrix}\!\diagdown\!\begin{matrix}\\NH\cdot CH_2\cdot CH_2\end{matrix}\!\diagup\!\begin{matrix}COOH\\\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.$$

The other substance of the formula $C_{20}H_{19}NO_9$ (*loc. cit.*, p. 84) melts at 178—179°, and is decomposed by warm dilute sodium carbonate into *hemipinic acid* and *ω-amidoethylpiperonylcarboxylic anhydride*. This substance must, therefore, be considered as the acid hemipinate of ω-amidoethylpiperonylcarboxylic anhydride, and its constitution is therefore :—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COO\text{—}\end{matrix}\!\begin{matrix}CO\text{———}\\NH_2\cdot CH_2\cdot CH_2\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.$$

Examination of Berberal, $C_{20}H_{17}NO_7$.

The experiments on the constitution of berberal were rendered extremely difficult from the fact that this substance is only produced in very small quantity in the oxidation of berberine; about 10 grams of pure substance was obtained from 1 kilo. of berberine hydrochloride.

The preparation and some of the properties of berberal have already been given in Part I of this research (pp. 81, 82), and it was there stated that this substance, although insoluble in alkalis in the cold, was apparently converted into the potassium salt of an acid by dissolution in potassium hydrate. In following up this reaction, it was found that, when treated with alcoholic potash, berberal yields three substances, namely: ω-amidoethylpiperonylcarboxylic anhydride ($C_{10}H_9NO_3$); an acid $C_{10}H_{10}O_5$ (m. p. 121°), and a neutral substance $C_{20}H_{19}NO_8$ (m. p. 149°); these are formed according to the following equations :—

$$C_{20}H_{17}NC_7 + H_2O = C_{20}H_{19}NO_8,$$
$$C_{20}H_{19}NO_8 = C_{10}H_9NO_3 + C_{10}H_{10}O_5.$$

As the constitution of ω-amidoethylpiperonylcarboxylic anhydride has already been proved (p. 997), there is no further need of discussing this compound here.

The acid $C_{10}H_{10}O_5$ is a monobasic acid forming salts of the formula $C_{10}H_9O_5M'$; it shows the following behaviour with reagents: (*a*) When treated with hydrogen iodide in Zeisel's apparatus, results were obtained which proved that the acid contained two methoxyl groups. (*b*) Fusion with potash converts the acid into protocatechuic acid; but if caustic potash solution (sp. gr. 1·4) is employed, and the acid simply digested with this in a reflux apparatus, veratric acid (m. p. 177—178°) and apparently also formic acid are produced, thus :—

$$C_{10}H_{10}O_5 + 2KOH = (CH_3O)_2C_6H_3COOK + HCOOK + H_2O$$

(*c*) When subjected to the action of hydroxylamine, an oxime, $C_{10}H_{11}NO_5$, is produced. This melts at about 124°, but at once becomes solid again, and then does not again melt until the temperature is raised to 213°. Further experiments showed that this behaviour was due to the formation of hemipinimide:—

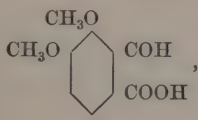
$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>NH.$$

This decomposition is represented by the equation

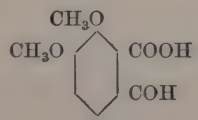
$$C_{10}H_{11}NO_5 = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>NH + H_2O.$$

(*d*) It is readily reduced by sodium amalgam, being converted into an acid, which when precipitated from its alkaline solution by the addition of mineral acids and recrystallised from water, loses 1 mol. of water, with formation of pseudomeconine, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH_2\\CO\end{matrix}>O$.

These experiments prove conclusively that the acid $C_{10}H_{10}O_5$ has the constitution represented by the formula I, and it thus bears a very close relationship to *opianic acid*, II—



I.



II.

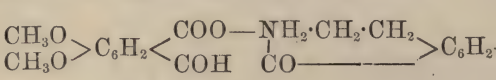
This relationship is brought out in a most interesting way by a parallel study of the reactions of the two substances; for instance, both are monobasic acids; both contain two methoxyl groups in the ortho-position; both, on reduction, yield meconines, and with hydroxylamine both yield oximes, which, when gently warmed, are converted into hemipinide. The acid $C_{10}H_{10}O_5$ may, therefore, be called *pseudopianic acid*.

The hydrolysis of berberal by means of dilute sulphuric acid was next studied, with the result that exactly similar decomposition products were formed in this case as in the hydrolysis by means of alcoholic potash, namely, the anhydride $C_{10}H_9NO_3$, pseudopianic acid, and the neutral substance $C_{20}H_{19}NO_6$.

Owing to the difficulty of obtaining any quantity of berberal, and the inadvisability of using up, for purely qualitative experiments, the small stock of this substance available, further information bearing on the constitution of this compound had to be in the first place obtained indirectly.

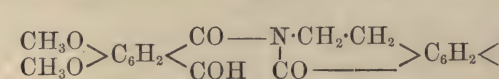
For this purpose a number of experiments on the action of opianic

acid (from narcotine) on the anhydride $C_{10}H_9NO_3$ were instituted and it was found that if these two compounds, in molecular proportions, are well mixed and dissolved in boiling water, a new substance, $C_{20}H_{19}NO_8$, crystallises out on cooling; this in its reactions shows very great similarity to the isomeric substance obtained from berberal, with which, however, it is not identical. The new compound is obviously the opianic salt of the anhydride $C_{10}H_9NO_3$, and its constitution is therefore represented by the formula

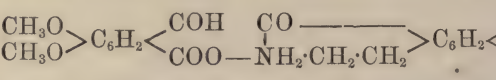


The most interesting property of this salt is that, when heated at 200°, it loses the elements of a molecule of water, and is converted into a compound $C_{20}H_{17}NO_7$ (m. p. 185°), which is isomeric with, and bears the strongest resemblance to berberal, for which reason I propose to name it *isoberberal*.

The constitution of this compound is represented by the formula

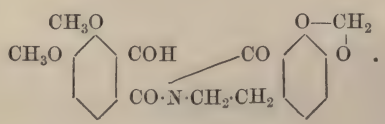


These experiments were next repeated with pseudopianic acid instead of opianic acid, with the result that exactly similar compounds were obtained. Pseudopianic acid and the anhydride $C_{10}H_9NO_3$ combine readily in aqueous solution with formation of the pseudopianic salt of the anhydride $C_{10}H_9NO_3$. This substance is identical with the compound $C_{20}H_{19}NO_8$, which is obtained by the action of alkalis on berberal. It is isomeric with the substance obtained by the action of opianic acid on the anhydride $C_{10}H_9NO_3$, and has the constitution represented by the formula



The relationship between these two substances is at once apparent from a comparison of their constitutional formulæ.

Just as the opianic salt of the anhydride $C_{10}H_9NO_3$, on heating at 180—200°, yields *isoberberal*, so this corresponding pseudopianate, under the same conditions, is converted almost quantitatively into berberal. *Berberal* has therefore the following constitutional formula:—



The synthesis of berberal may be still more conveniently accomplished by heating an intimate mixture of pseudopianic acid and the anhydride $C_{10}H_9NO_3$, in molecular proportion, at 200° for a few minutes. The reaction which takes place under these circumstances is the following:—

$$C_{10}H_{10}O_5 + C_{10}H_9NO_3 = C_{20}H_{17}NO_7 + H_2O.$$

There is a possibility of synthesising berberine from berberal, and if this were to succeed, a most interesting isomeric alkaloïd could be obtained from isoberberal. Experiments on this point are in progress.

Oxyberberine, $C_{20}H_{17}NO_5$.—This substance, which is formed only in very small quantities by the oxidation of berberine under the conditions described in this paper, is insoluble in alkalis, but combines with strong acids, forming salts; its basic properties are, however, very much less marked than those of berberine itself.

Oxyberberine is a tertiary base, incapable of forming an acetyl compound. It does not appear to combine with phenylhydrazine; it is not decomposed on boiling with alcoholic potash or on heating with alcoholic ammonia at 150°.

Dioxyberberine, $C_{20}H_{17}NO_6$.—This extremely interesting substance has scarcely any basic properties, but it dissolves in warm alcoholic potash, forming a deep-red solution; this, on cooling, deposits a beautiful, crystalline potassium salt, $C_{20}H_{18}NO_7K$, which is decomposed by acids with regeneration of dioxyberberine. In contact with oxygen or air, the solution of the potassium salt gradually loses its red colour, and in the course of a few days becomes almost colourless; on the addition of acids it then deposits a white precipitate of berberilic acid. This remarkable reaction may be represented by the equation

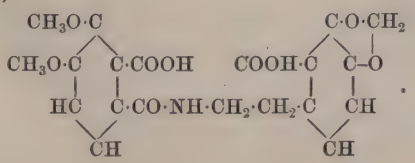
$$C_{20}H_{18}NO_7K + KOH + O_2 = C_{20}H_{17}NO_8K_2 + H_2O.$$

Further experiments will, it is hoped, throw some light on this very peculiar reaction.

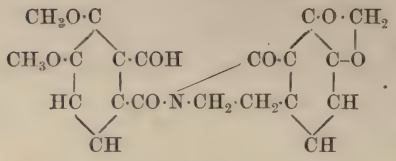
Constitution of Berberine.—Although not conclusively proved by the above experiments, the constitution of berberine may be deduced with a considerable amount of certainty from the results obtained in the study of the constitution of berberilic acid and of berberal.

These two substances have the following constitutional formulæ:—

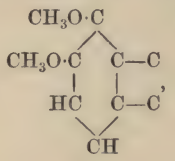
Berberilic acid,

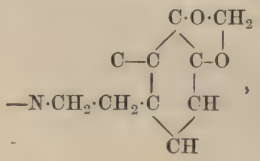


Berberal,



From an examination of these formulæ, it is readily seen that berberine, $C_{20}H_{17}NO_4$, must contain the following groups of atoms:—

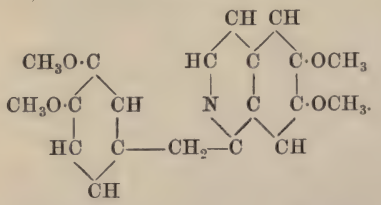




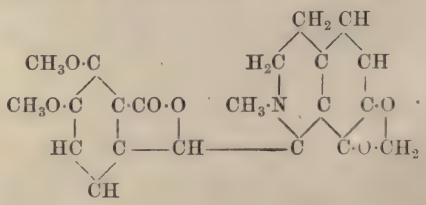
and as these already contain C_{20}, H_{16}, N, O_4, it follows that, in assigning a constitutional formula to berberine, these two parts must be united with the addition of one atom of hydrogen only.

As the decomposition products of berberine are in many respects very similar to those obtained from papaverine, hydrastine, and narcotine, it is reasonable to suppose that these four alkaloïds are all very closely related in constitution. The following formulæ are generally accepted as representing the constitution of papaverine, hydrastine, and narcotine:—

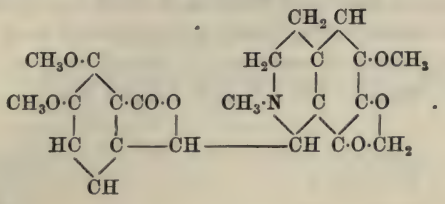
Papaverine (Goldschmiedt, *Monatsh.*, **6**, 667),



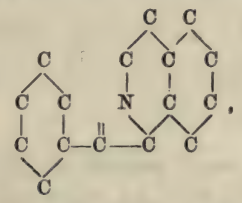
Hydrastine (Freund and Rosenberg, *Ber.*, **23**, 414),



Narcotine (Roser, *Annalen*, **254**, 357),

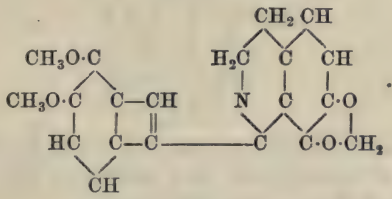


These alkaloïds are all built upon the common foundation

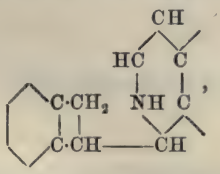


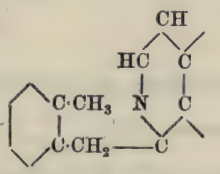
and a careful study of the properties of berberine and its derivatives leaves scarcely any doubt that this group of atoms or one very similar occurs also in berberine.

With this point in view, the simplest formula for berberine would be



Berberine, when reduced, yields *tetrahydroberberine*, $C_{20}H_{21}NO_4$. This substance is a tertiary base. On treatment with oxidising agents (bromine, iodine, nitric acid, &c.), it is very readily reconverted into berberine; its constitution cannot therefore be derived from the above formula, as this, on reduction, would yield a compound which would contain one of the following two groups:—



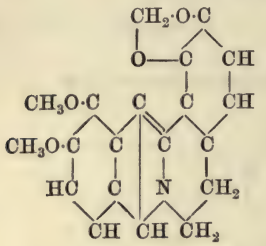


A substance containing the former would be a secondary base, and a

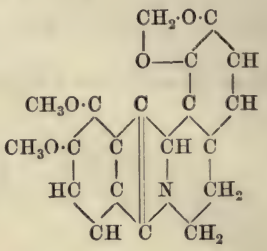
compound containing the latter would obviously not be reconverted into the alkaloïd on treatment with such oxidising agents as iodine.

There are, however, two formulæ, closely allied to the one given above, and built upon a very similar foundation, which account, in a satisfactory manner, for all the known reactions of berberine, namely :—

I.

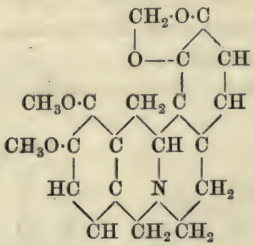


II.



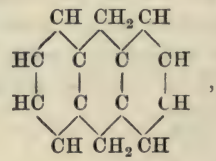
and, of these, formula I would seem to be the more plausible.

Both of these formulæ yield, on reduction, the same tetrahydroberberine :—



This formula accounts at once for the ready way in which tetrahydroberberine is reconverted into berberine on oxidation, as is apparent from the following considerations :—

In the first place, this formula contains a group of atoms very similar to that contained in hydranthracene,

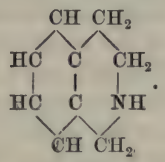


and this substance, on oxidation, is converted with the greatest ease into anthracene, $C_6H_4<\begin{matrix}CH\\|\\CH\end{matrix}>C_6H_4$.

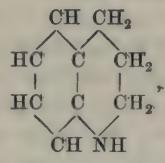
This point is still more clearly brought out from the comparison of the above formula for tetrahydroberberine with that of dihydro-

acridine,* $C_6H_4<\overset{CH_2}{NH}>C_6H_4$, a substance which, when treated even with such feeble oxidising agents as alcoholic nitrate of silver, loses two atoms of hydrogen with formation of acridine, $C_6H_4<\overset{CH}{\underset{N}{\|}}>C_6H_4$. From these considerations, it would appear at first sight as though tetrahydroberberine, $C_{20}H_{21}NO_4$, should, on oxidation, lose only two atoms of hydrogen with formation of a substance of the formula $C_{20}H_{19}NO_4$.

Tetrahydroberberine is, however, a derivative of tetrahydroisoquinoline,



This substance has lately been prepared by Hoogewerff and Van Dorp (*Recueil des travaux chimiques des Pays-Bas*, **5**, 310), and has been found to be readily oxidised even by nitrate of silver, but the products of the oxidation have not yet been studied. On the other hand, tetrahydroquinoline,



which is very closely related to tetrahydroisoquinoline, is readily oxidised by bromine or dilute chromic acid solution to quinoline and its derivatives.

It is interesting to note that berberine itself contains a dihydroisoquinoline group, and the presence of this group accounts for the fact that the alkaloïd reduces nitrate of silver, and is so readily attacked by oxidising agents.

It is hoped that further experiments, which are in progress, will succeed in removing the two hydrogen atoms; and that in this way the mother substance of berberine, that is,

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\overset{C=C\text{———}}{\underset{CH\cdot N\cdot CH:CH}{\|}}>C_6H_2<\overset{O}{\underset{O}{\|}}>CH_2,$$

may be obtained.

* See also dihydrophenylacridine (Bernthsen, *Annalen*, **224**, 25), and methylhydrophenylacridine (Bernthsen, Bender, *Ber.*, **16**, 1815).

Assuming formula I (p. 1006) to represent the constitution of berberine, the constitution of oxyberberine and dioxyberberine is readily understood from the following formulæ:—

Oxyberberine, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH{=}C\\CO{-}N{\cdot}CH_2{\cdot}CH_2\end{matrix}>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2.$

Dioxyberberine, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO{-}CH\\CO{-}N{\cdot}CH_2{\cdot}CH_2\end{matrix}>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2.$

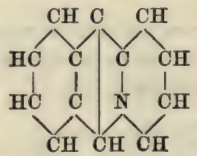
These formulæ explain the general character and reactions of these substances, and give a clear insight into the processes which take place in the production of these compounds from berberine, and in the subsequent splitting up of the central oxidised ring with formation of berberal and anhydroberberilic acid.

The dioxyberberine formula also explains the fact that this substance, on treatment with alcoholic potash, yields a potassium salt of the formula $C_{20}H_{18}NO_7K$; this would have the constitution

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO{-}CH\\COOK\quad NH{\cdot}CH_2{\cdot}CH_2\end{matrix}>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2.$$

It is, however, difficult to account for the conversion of this salt into a salt of berberilic acid by the absorption of oxygen in alkaline solution.

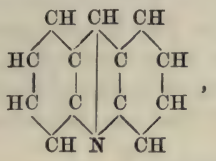
With the introduction of each oxygen atom into the molecule of berberine, the basic nature of the substance, and at the same time the intensity of its colour, decreases, until, as soon as the central ring is split, as in the case of berberal and anhydroberberilic acid, the derivatives become colourless, and show no appreciable basic properties. On the other hand, the methoxy-groups and the methylenedioxy-group appear to have little influence on the tinctorial property of berberine, because other alkaloïds, such as narcotine and hydrastine, which are somewhat similarly constituted, and contain the same number, or even more, of such groups, are colourless. The group of atoms which appears to impart to berberine its intense yellow colour and tinctorial properties is the strongly basic group



which is absent in the colourless alkaloïds papaverine, hydrastine, and narcotine. This group does not appear to have yet been investigated; but there are, on the other hand, a number of substances which contain groups of atoms very closely allied to this, and it is

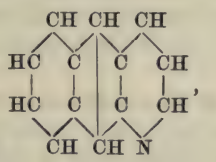
interesting to note that the salts of such substances, like those of berberine, are intensely yellow. The following instances, taken from a large number, will illustrate this point.

The whole series of *acridine* derivatives which contain the group



although sometimes colourless themselves, invariably yield intensely yellow salts.

α-Phenyl-α-naphthaquinoline, $C_{10}H_6<\begin{matrix}C{:}HCH\\ N{=}C{-}C_6H_5\end{matrix}$, which contains the very similarly constituted group,



is yellow, and its salts are also intensely yellow. These instances might be multiplied to a considerable extent. It appears therefore that the formula proposed for berberine is in harmony with the fact that the alkaloïd is so intensely yellow. In Part I of this research (*loc. cit.*, p. 88), a substance is described, which results from the action of hydriodic acid on berberine, and which was termed berberoline. This compound (of which the sulphate was analysed) was then thought to have the composition $C_{18}H_{11}NO_2(OH)_2$. It is, however, evident that this formula cannot be correct, as it is obviously produced from berberine by the elimination of the methylene and the methyl groups, thus :—

$$C_{20}H_{17}NO_4 + 4HI = C_{17}H_9N(OH)_4 + CH_2I_2 + 2CH_3I.$$

The analysis already given agrees well with the new formula.

The constitution of *berberoline* is represented by the formula

$$\begin{matrix}HO\\HO\end{matrix}>C_6H_2<\begin{matrix}C{=}C\\CH{\cdot}N{\cdot}CH_2{\cdot}CH_2\end{matrix}>C_6H_2<\begin{matrix}OH\\OH\end{matrix}.$$

In the experimental part of this paper, a number of substances are described, some of which afford additional evidence as to the constitution of berberine, others, at first sight, appear to have little connection with this problem; but it must be borne in mind that

these new compounds were prepared and examined at a time when very little was known as to the constitution of the alkaloïd, and when their examination appeared likely to give important clues to the nature of the various complicated substances which were obtained from time to time.

I cannot conclude this part of the paper without expressing my thanks to Mr. Bertram Prentice for the very valuable assistance which he rendered, especially in the preparation of the large amount of material necessary for these experiments.

Oxidation of Berberine with Potassium Permanganate.

In continuing the investigation of the action of potassium permanganate on berberine, special care was taken that the berberine hydrochloride employed was pure, so that no doubt should exist that all the substances subsequently obtained were actually derived from berberine itself, and not from a small quantity of some other alkaloïd admixed therewith.

Commercial berberine hydrochloride, obtained from Merck, in Darmstadt, was first recrystallised from water, then dissolved in water, and the solution boiled with a small quantity of pure precipitated calcium carbonate for a few minutes; the liquid, originally of a yellow colour, is rendered distinctly brownish by this treatment, but the filtered solution, on cooling, deposits long, light brown needles of almost pure berberine hydrochloride, and these, after well washing and drying on a porous plate for some days at the ordinary temperature, gave the following numbers on analysis:—

I. 0·1484 gram substance gave 0·0806 gram H_2O and 0·2950 gram CO_2.

0·5249 gram substance heated with nitrate of silver and nitric acid in a sealed tube gave 0·1592 gram AgCl.

0·3354 gram substance gave 9·5 c.c. N.; $t = 16°$; bar. = 740 mm.

II. 0·1956 gram substance gave 0·1058 gram H_2O and 0·3884 gram CO_2.

	Theory. $C_{20}H_{17}NO_4HCl + 4H_2O$.	Found. I.	Found. II.
C.....	54·13 per cent.	54·21	54·15 per cent.
H	5·86 „	6·03	6·03 „
Cl.....	7·98 „	7·62	— „
N	3·16 „	3·21	— „

Although the crystals obtained by this treatment are slightly brownish, this method of purification was almost always employed.

Recrystallisation first from dilute alcohol, and then from very dilute hydrochloric acid, entirely removes the brownish tinge, and the crystals have then a fine yellow colour and satiny lustre. In investigating the products formed by the oxidation of berberine by potassium permanganate, the following were the quantities usually employed :—

Berberine hydrochloride	7 grams.
Potassium permanganate	9 „
Dry potassium carbonate	1 „

In those cases, however, where an increased yield of some one of the oxidation products was desired, these quantities were varied, proportions more favourable to the formation of that particular product being employed, as will be mentioned in the description of the individual substances. The berberine hydrochloride was dissolved in about half a litre of water, at a temperature of about 70°, the potassium carbonate added, and then the strong hot solution of the permanganate, in half a litre of water, run in moderately rapidly, either drop by drop, or in a very fine stream from a tap funnel. The product from a large number of such operations was well cooled, treated with sulphurous anhydride (as explained in Part I, p. 77), and thus separated into a yellow, flocculent *precipitate* and a yellowish-coloured *solution*. The treatment of the *precipitate* was as follows :—The yellow, amorphous mass was thoroughly washed by grinding up with water, filtering through cloth, and squeezing; this operation being repeated at least three times, and the washings always added to the original *solution*. The *precipitate*, which, after drying on a porous plate, amounts to about 40 per cent. of the berberine hydrochloride used, was treated with dilute sodium carbonate solution, substantially in the same way as previously described (Part I, pp. 77–78), and thus separated into two portions :—

I. *Soluble in Sodium Carbonate.*—This contains the acid $C_{20}H_{19}NO_9$ (α-berberilic acid), and a certain amount of the substance $C_{20}H_{17}NO_8$ (anhydroberberilic acid). Both of these compounds have been already described (Part I, pp. 78–80).

II. *Insoluble in Sodium Carbonate.*—This portion is further resolved by boiling with acetic acid into *anhydroberberilic* acid, $C_{20}H_{17}NO_8$ (see p. 1037); *berberal*, $C_{20}H_{17}NO_7$ (see p. 1062); and berberine hydrogen sulphite, $C_{20}H_{17}NO_4,H_2SO_3$ (see p. 1097).

The *solution*, which in bulk frequently amounted to 150—200 litres, was rapidly evaporated in large, flat, enamelled iron pans, until its volume had been reduced by about one half. During the

evaporation a quantity of a yellow, flocculent substance separated, consisting for the most part of inorganic salts, but containing also, as examination showed, a considerable quantity of organic matter. This precipitate was collected on cloth bags, washed with water, transferred to a large evaporating basin, and gently warmed with a considerable bulk of 5 per cent. hydrochloric acid; quantities of sulphurous anhydride were evolved, and the greater part of the substance went into solution. The insoluble matter was collected, washed with water, and treated with very dilute hydrochloric acid, until the resulting yellow mass contained only traces of inorganic matter. This crude substance contains, besides varying quantities of anhydroberberilic acid, two new compounds, $C_{20}H_{17}NO_5$ (oxyberberine, p. 1085) and $C_{20}H_{17}NO_6$ (dioxyberberine, p. 1087); the methods of separation of these are given on pp. 1083–4.

The liquors from which this insoluble matter had been separated were again concentrated to half their bulk, allowed to cool, the inorganic salts which separated discarded, and the evaporation carefully continued until slight decomposition took place, as shown by rapid discoloration accompanied by empyreumatic odours. The liquor was transferred to large bottles, and extracted at least 20 times with ether, the separation of the two liquids being effected by syphoning off the aqueous layer. The colourless ethereal solution, which has a strong blue fluorescence, was evaporated in a large flask, and the semi-solid residue (about 35 grams from each kilo. of berberine hydrochloride used), which contains the substance $C_{20}H_{19}NO_9$ (see Part I, p. 84), hemipinic acid, and other products was treated as follows:—About $\frac{3}{4}$ litre of hot water was added, the whole heated on a sand-bath for five minutes, with sufficient sodium carbonate to make the solution decidedly alkaline, and the liquid rapidly filtered through a jacketed funnel. A small quantity of a dirty grey, insoluble substance (see p. 1094) which contained hemipinic anhydride was left on the paper.

The alkaline solution on cooling deposited a considerable quantity (about 13—14 grams) of beautiful, leafy crystals of a new substance, $C_{10}H_9NO_3$ (ω-amidoethylpiperonylcarboxylic anhydride), an exhaustive examination of which is given on p. 1013. The filtrate from these crystals was concentrated, allowed to stand 48 hours, so as to completely deposit any further quantities of the anhydride, $C_{10}H_9NO_3$, filtered, acidified with dilute hydrochloric acid, and gently warmed. A small quantity of a greyish substance which contained a new acid, $C_{20}H_{15}NO_8$ (berilic acid), remained undissolved, and was removed by filtration (see p. 1091).

The filtrate from this was repeatedly extracted with ether, and the ethereal solution evaporated, when a quantity of a yellowish semi-

solid mass remained. This contains hemipinic acid, $C_{10}H_{10}O_6$, and hydrastic acid, $C_9H_8O_6$; the method of separation and purification of these acids is given on p. 1095.

The original concentrated solution which had been extracted with ether contains, besides the bulk of the inorganic salts, large quantities of organic matter, which appears to consist for the most part of hemipinic acid, together with varying quantities of the anhydride, $C_{10}H_9NO_3$, mentioned above.

The examination of these liquors is given on p. 1105. A long series of operations such as those involved in the separation of the numerous oxidation products of berberine is difficult to follow from mere description, and I have thought that it might facilitate reference if the methods employed were summarised in tabular form (p. 1014).

The following pages contain a detailed examination of the substances obtained from berberine by oxidation, as explained in the preceding pages.

ω-Amidoethylpiperonylcarboxylic Anhydride,

$$C_{10}H_9NO_3 = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\ -NH\\ |\\ CH_2-CH_2\end{matrix}.$$

The crude product, the preparation of which is given on p. 1012, is readily purified by recrystallisation from boiling water, and is thus obtained in beautiful, colourless plates, which, after drying at 100°, gave the following results on analysis:—

I. 0·1196 gram substance gave 0·0554 gram H_2O and 0·2753 gram CO_2.

0·1476 gram substance gave 9·1 c.c. N; $t = 17$; bar. = 740 mm.

II. 0·1370 gram substance gave 0·0600 gram H_2O and 0·3143 gram CO_2.

	Theory. $C_{10}H_9NO_3$.	Found. I.	Found. II.
C	62·82 per cent.	62·77	62·56 per cent.
H	4·71 „	5·15	4·79 „
N.....	7·33 „	7·23	— „

This beautiful substance melts at 181—182°; when rapidly heated in small quantities in a test tube, it distils with only slight decomposition, and the oily distillate, on cooling, solidifies to a mass of colourless plates. It is very sparingly soluble in cold, but readily in hot water, the hot solution, on cooling, depositing beautiful, very characteristically shaped crystals, often grouped together in masses

Berberine Hydrochloride is Oxidised with Potassium Permanganate, the Product treated with Sulphurous Anhydride, (*see p.* 1011) *and Filtered.*

Yellow precipitate treated with warm dilute sodium carbonate solution and filtered.

Residue boiled with acetic acid and filtered hot.

Residue contains **Berberine hydrogen sulphite,** $C_{20}H_{17}NO_4H_2SO_3$ (p. 1097).

Solution on cooling deposits crystals which are separated by filtration.

Residue consists of **Anhydroberberilic acid,** $C_{20}H_{17}NO_8$ (p. 1037).

Solution contains **Berberal,** $C_{20}H_{17}NO_7$ (p. 1062).

Solution contains **Berberilic acid,** $C_{20}H_{19}NO_9$, and some **Anhydroberberilic acid,** $C_{20}H_{17}NO_8$ (p. 1037).

Yellow filtrate evaporated to half its bulk and filtered.

Precipitate contains **Oxyberberine,** $C_{20}H_{17}NO_5$ (p. 1085). **Dioxyberberine,** $C_{20}H_{17}NO_6$ (p. 1087). **Anhydroberberilic acid,** $C_{20}H_{17}NO_8$ (p. 1037).

Solution evaporated to half its bulk and extracted 20 times with ether.

Ethereal solution evaporated, residue boiled with dilute sodium carbonate solution and filtered hot.

Residue contains **Hemipinic anhydride,** $C_{10}H_8O_5$ (p. 1094).

Solution allowed to cool and filter.

Crystals of **ω-Amidoethylpiperonylcarboxylic anhydride,** $C_{10}H_9NO_3$ (p. 1013).

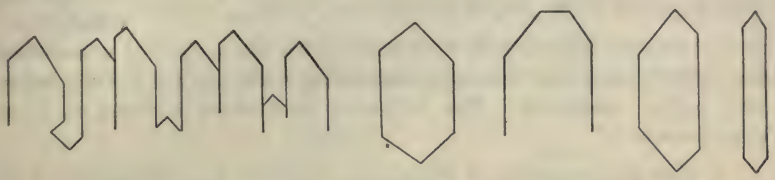
Solution acidified with hydrochloric acid and filtered.

Residue contains **Berilic acid,** $C_{20}H_{15}NO_8$ (p. 1091).

Solution contains **Hydrastic acid,** $C_9H_6O_6$, and **Hemipinic acid,** $C_{10}H_{10}O_6$ (p. 1095).

Aqueous solution contains **Hemipinic acid,** $C_{10}H_{10}O_6$, **ω-Amidoethylpiperonylcarboxylic anhydride,** $C_{10}H_9NO_3$, and inorganic salts (p. 1105).

very much resembling the teeth of a saw. These, when examined under the microscope, present the following appearance:—



It is very readily soluble in warm methyl alcohol; the warm solution, on slowly cooling, or, better still, on spontaneous evaporation, deposits well-formed, tabular crystals, which have a beautiful lustre. When examined under the microscope, these are seen to have forms almost exactly similar to those drawn above, the only difference being that the crystals from methyl alcohol were single examples and very well shaped, twins being almost entirely absent.

The anhydride $C_{10}H_9NO_3$ is also readily soluble in ethyl alcohol and in boiling benzene, xylene, or toluene, extremely soluble in chloroform and acetic acid, sparingly in ether, and almost insoluble in light petroleum. It crystallises from hot benzene in long, flat, ill-shaped plates. Its hot dilute aqueous solution gives no precipitate with mercuric chloride, but, on cooling, beautiful, colourless needles of a double compound separate. These are readily soluble in boiling water.

With a solution of phosphomolybdic acid, an aqueous solution of the anhydride $C_{10}H_9NO_3$, acidified with hydrochloric acid, even when very dilute, gives a yellowish-white precipitate, which dissolves appreciably in boiling water.

The anhydride $C_{10}H_9NO_3$ is insoluble in caustic potash solution, even on boiling; it dissolves readily in strong acids, forming salts, which, however, are very unstable, and could not be obtained in a state fit for analysis. From hot dilute acids, the substance crystallises unchanged.

Fusion of the Anhydride $C_{10}H_9NO_3$ *with Potash.*—Although it is not dissolved on boiling with strong solutions of potassium hydrate, the compound is readily decomposed by fusion with potash. It first of all melts to an oil, ammoniacal vapours are given off, and in a short time a clear, slightly brownish melt is formed. This is soluble in water, producing a purplish solution, which changes colour in the way so characteristic of a protocatechuic acid melt, and on acidifying and extracting with ether, a semi-solid mass is obtained, which shows the ferric chloride and other reactions of catechol or protocatechuic acid, and probably consists of a mixture of both these substances.

Attempts to obtain a Methyl Derivative of the Anhydride $C_{10}H_9NO_3$.—As already mentioned in the Introduction, the substance $C_{10}H_9NO_3$ is closely related to oxyhydrastinine, $CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2}$, and numerous experiments were made with the object of converting the former into the latter by treatment with methyl iodide under very varied conditions. The following is a short account of these experiments:—

1. The finely powdered substance $C_{10}H_9NO_3$ was heated for four hours with a large excess of methyl iodide in a flask connected with a reflux apparatus. The methyl iodide was then distilled off, and the residue recrystallised from water. The crystals obtained melted at 182—183°, and consisted of unchanged substance.
2. The substance $C_{10}H_9NO_3$ was dissolved in alcohol and heated at 100° with excess of methyl iodide in a sealed tube for five hours. No action took place.
3. 2 grams of the substance $C_{10}H_9NO_3$ was dissolved in a solution of 0·6 gram of caustic potash in pure methyl alcohol, 2 grams of methyl iodide added, and the mixture heated in a sealed tube at 100° for five hours. On cooling, a quantity of the unchanged substance separated, and from the solution the remainder was readily obtained by distilling off the alcohol and adding water.
4. 1·2 grams of the substance $C_{10}H_9NO_3$ was dissolved in a solution of sodium methoxide (containing 2 grams of sodium) and heated with 8 grams of methyl iodide at 140° for five hours. The clear solution was evaporated, the residue dissolved in a little cold water, acidified, and extracted with ether. A yellowish oil, readily soluble in water, was obtained; the solution gave with ferric chloride a dark-green coloration, showing that decomposition of the methylene-dioxy-group, $CH_2<^{O}_{O}$, had taken place (see footnote, p. 996).

Acetyl-ω-amidoethylpiperonylcarboxylic Anhydride,

$C_{12}H_{11}NO_4 = CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N(C_2H_3O)}_{CH_2\cdot CH_2}$ or $CH_2<^{O}_{O}>C_6H_2<^{C(OC_2H_3O):N}_{CH_2\text{———}CH_2}$.

In order to prepare this substance, the pure anhydride $C_{10}H_9NO_3$ was dissolved in acetic anhydride and the solution boiled for four hours in a flask connected with a reflux apparatus. The excess of

acetic anhydride and acetic acid was distilled off until only a small quantity of liquid remained, and this on cooling almost completely solidified to a cake of crystals. These were collected, well drained on a porous plate, dried at 110°, and analysed, with the following result:—

0·1578 gram substance gave 0·0692 gram H_2O and 0·3590 gram CO_2.

	Theory. $C_{12}H_{11}NO_4$.	Found.
C	61·80 per cent.	62·04 per cent.
H	4·72 „	4·87 „

This acetyl derivative crystallises from acetic anhydride in colourless needles which melt at 128—130°. It is readily hydrolysed on boiling with acids or alkalis, and, in order to further prove its constitution, a weighed quantity was hydrolysed and the amount of acetic acid produced estimated.

1·1086 gram substance was boiled with 30 per cent. sulphuric acid until completely dissolved, and the liquid distilled, with the addition of water when necessary, until the distillate no longer showed acid reaction.

The distillate required for complete neutralisation 49·7 c.c. of standard potassium hydrate solution (1 c.c. of which = 0·00597 c.c. acetic acid). 0·2967 gram of acetic acid was therefore produced, = 26·76 per cent. $C_{12}H_{11}NO_4$ on hydrolysis should yield 25·75 per cent. of acetic acid.

Amidoethylbromopiperonylcarboxylic Anhydride,

$$C_{10}H_8BrNO_2 = CHBr<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot NH\\ |\\ CH_2\cdot CH_2\end{matrix}(?).$$

When treated with bromine, the anhydride $C_{10}H_9NO_3$ is readily attacked, one atom of bromine replacing one atom of hydrogen in the molecule, forming a compound of the formula $C_{10}H_8BrNO_3$. As the bromine atom in this compound is very readily removed by nitric acid and silver nitrate, it can scarcely be situated in the benzene ring, and it is probable that the substitution takes place in the methylene dioxy-group, and that the compound has the constitutional formula given to it above.

The compound $C_{10}H_8BrNO_3$ is readily prepared by exposing finely-powdered ω-amidoethylpiperonylcarboxylic anhydride, $C_{10}H_9NO_3$, (p. 1013) to the action of a large excess of bromine vapour, under a bell jar, in direct sunlight. After standing for two days, the original white powder has become converted into a dark-brown syrup; this, on exposure to a current of air, loses its excess of bromine, yielding

an ochre-coloured mass. This crude substance is best purified by repeated recrystallisation from boiling amyl alcohol, from which it is deposited on cooling in light-yellow, feathery crystals; these, after washing first with amyl alcohol and then with methyl alcohol and drying at 105°, gave the following results on analysis:—

0·2003 gram substance gave 0·0564 gram H_2O and 0·3294 gram CO_2.

0·2240 gram substance, heated with nitric acid and silver nitrate in a sealed tube at 130—140°, gave 0·1543 gram AgBr.

	Theory. $C_{10}H_8BrNO_3$.	Found.
C	44·44 per cent.	44·85 per cent.
H.....	2·97 „	3·12 „
Br.....	29·63 „	29·38 „

The bromo-derivative melts at 238—240°. It is readily soluble in chloroform, in boiling acetic acid, and in amyl alcohol; moderately soluble in hot xylene and alcohol, sparingly in carbon bisulphide, benzene, and light petroleum. It crystallises from amyl alcohol or xylene in slender, pale-yellow needles. It is readily decomposed by nitric acid and silver nitrate at ordinary temperatures, with separation of silver bromide.

Nitrosoamidoethylpiperonylcarboxylic Anhydride,

$$C_{10}H_8N(NO)O_3 = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot N\cdot NO\\ |\\ CH_2\cdot CH_2\end{matrix}.$$

When treated with nitrous acid, the anhydride $C_{10}H_9NO_3$ (p. 1013) behaves as a secondary base, yielding a well-defined and very characteristic nitroso-derivative according to the equation

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot NH\\ |\\ CH_2\cdot CH_2\end{matrix} + NOOH = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot N\cdot NO\\ |\\ CH_2\cdot CH_2\end{matrix} + H_2O.$$

In preparing this substance the following quantities were found to give good results:—

$C_{10}H_9NO_3$ (finely powdered)	3 grams.
Hydrochloric acid (sp. gr. 1·1)	100 c.c.
Water	75 „
Solution of sodium nitrite containing 10 grams $NaNO_2$ in 100 c.c. water.....	15 „

The substance $C_{10}H_9NO_3$ is first dissolved in the hydrochloric acid (this being readily accomplished by warming gently on a water-

bath), the water is then added, the solution rapidly cooled to 20°, and lastly, the nitrite solution is run in, the flask being well cooled during the operation. The first few drops of the nitrite cause the solution to acquire a deep reddish-brown colour; this, however, soon disappears, and is succeeded by the separation of a yellow, amorphous precipitate, which ultimately causes the liquid to become quite thick. The whole operation must be quickly performed, otherwise the substance $C_{10}H_9NO_3$ is apt to crystallise out of the hydrochloric acid, and thus escape the action of the nitrous acid.

After standing for some time, the precipitate is collected, washed several times with water, dried on a porous plate, and recrystallised once or twice from alcohol. The pure substance is thus obtained in long, deep-yellow needles, which on analysis gave the following numbers:—

0·1575 gram substance gave 0·0580 gram H_2O and 0·3150 gram CO_2.

0·1003 gram substance gave 10·7 c.c. N; $t = 17°$; bar. = 760 mm.

	Theory. $C_{10}H_8N(NO)O_3$.	Found.
C	54·54 per cent.	54·55 per cent.
H.....	3·63 „	4·04 „
N.....	12·73 „	12·70 „

This interesting substance crystallises from alcohol in beautiful, long, glistening, yellow needles or four-sided prisms which melt at 194—195° with decomposition. It is readily soluble in boiling alcohol, chloroform, and benzene, almost insoluble in water or light petroleum, and very sparingly soluble in bisulphide of carbon. The solubility of this compound in solvents is very much influenced by its condition, the amorphous substance being far more readily dissolved than the crystalline variety. It is insoluble in acids and alkalis in the cold, but it dissolves readily in warm dilute sodium hydrate solution with evolution of nitrogen and formation of a salt of ω-hydroxyethylpiperonylcarboxylic acid, thus:—

$$CH_2\langle{}^{O}_{O}\rangle C_6H_2\langle{}^{CO\cdot N\cdot NO}_{CH_2\cdot CH_2} + NaOH =$$

$$CH_2\langle{}^{O}_{O}\rangle C_6H_2\langle{}^{COONa}_{CH_2\cdot CH_2\cdot OH} + N,$$

a decomposition which is described in detail on p. 1020.

The least trace of the nitroso-derivative, when treated with phenol and two drops of sulphuric acid, gives a red solution, which, on the addition of excess of dilute alkali, changes to a beautiful blue (Liebermann's nitroso-reaction).

The nitroso-compound seems to be readily reduced in alcoholic solution by tin and hydrochloric acid, the original yellow solution becoming almost colourless. No attempts were made to isolate the reduction product.

ω-Hydroxyethylpiperonylcarboxylic Acid, $C_{10}H_{10}O_5$ = $CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2\cdot OH}$, *and its Anhydride*, $C_{10}H_8O_4$ = $CH_2<^{O}_{O}>C_6H_2<^{CO\cdot O}_{CH_2\cdot CH_2}$.

As mentioned in the last paragraph, the nitroso-derivative, $C_{10}H_8N(NO)O_3$, is readily decomposed by boiling with alkalis with evolution of nitrogen, and formation of a salt of a new acid, $C_{10}H_{10}O_5$. The latter, on the addition of an acid, is precipitated in the form of slender, white needles, which are somewhat difficult to purify on account of the ease with which they are converted into the inner anhydride $C_{10}H_8O_4$, thus:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2\cdot OH} = CH_2<^{O}_{O}>C_6H_2<^{CO\cdot O}_{CH_2\cdot CH_2} + H_2O.$$

The best results were obtained by employing the crude amorphous nitroso-compound, as obtained directly by the action of sodium nitrite on the hydrochloric acid solution of the substance $C_{10}H_9NO_3$ (see p. 1019), as this is much more readily acted on by alkalis than is the crystalline product.

The yellow precipitate is well washed, mixed with a considerable quantity of water (3 grams of nitroso-compound to 100 c.c. of water), transferred to a porcelain basin, sufficient sodium hydrate added to make the liquid very distinctly alkaline, and the whole gently heated on a water bath. In a short time decomposition sets in, and the nitroso-compound rapidly disappears, considerable quantities of nitrogen being evolved. The product, if not quite clear, is filtered, well cooled, acidified with hydrochloric acid, and allowed to stand for about half an hour. The white, crystalline precipitate, which consists of the nearly pure acid $C_{10}H_{10}O_5$, is collected and well washed with small quantities of water, care being taken to preserve all the aqueous solutions, as these, when extracted with ether, yield further quantities of the acid. The purification of the acid $C_{10}H_{10}O_5$ is best accomplished by first converting it into its anhydride, $C_{10}H_8O_4$, recrystallising this several times, and then reconverting the pure anhydride into the acid by dissolving it in alkali, and reprecipitating with hydrochloric acid.

For this purpose, the crude acid is dissolved in the least possible

quantity of boiling water, the solution gently boiled for about five minutes, and rapidly filtered through a jacketed funnel. The hot liquid, on cooling, deposits beautiful, glistening, colourless crystals of the anhydride $C_{10}H_8O_4$, which by recrystallisation from water are readily obtained pure. For analysis, the substance was dried at 105°.

I. 0·1582 gram substance gave 0·0614 gram H_2O and 0·3620 gram CO_2.

II. 0·1418 gram substance gave 0·0540 gram H_2O and 0·3252 gram CO_2.

	Theory. $C_{10}H_8O_4$.	Found. I.	Found. II.
C	62·50 per cent.	62·40	62·54 per cent.
H	4·17 „	4·31	4·23 „
O	33·33 „	33·29	33·23 „

This anhydride, $C_{10}H_8O_4$, melts at 126—127°, and distils without decomposition when heated in small quantities. It is readily soluble in boiling water, and the hot solution on cooling deposits the substance in the form of beautiful, glistening crystals, which, however, as a rule, are ill-defined. It is sparingly soluble in cold water, and is readily extracted from its solution by ether. It is, further, readily soluble in alcohol, ether, and acetic acid, excessively soluble in chloroform. It dissolves sparingly in cold benzene and light petroleum.

The anhydride $C_{10}H_8O_4$ is insoluble in alkaline carbonates in the cold, and is only very slowly dissolved on boiling, but it dissolves in ammonia, and much more readily in potassium hydrate solution with formation of the potassium salt of the acid $C_{10}H_{10}O_5$,

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix} + KOH = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOK\\CH_2\cdot CH_2\cdot OH\end{matrix}$$

In studying this reaction, the pure anhydride $C_{10}H_8O_4$ was ground up with a little water into a thin paste, a few drops of a clear solution of potassium hydrate added, and the whole gently warmed until complete solution had taken place. The solution was nearly neutralised with dilute hydrochloric acid, well cooled, an excess of acid added, the white, crystalline substance which separated collected, well washed with water, and dried on a porous plate, first at the ordinary temperature and then for a few minutes at 80°.

Analysis:—

0·1199 gram substance gave 0·0528 gram H_2O and 0·2510 gram CO_2.

	Theory. $C_{10}H_{10}O_5$.	Found.
C	57·14 per cent.	57·09 per cent.
H	4·77 „	4·87 „
O	38·09 „	38·04 „

ω-Hydroxyethylpiperonylcarboxylic acid melts at 146°, and is at the same time decomposed into its anhydride, $C_{10}H_8O_4$, and water. It is readily soluble in hot water, but sparingly so in cold. It may be recrystallised from warm water if the operation be quickly carried out, but boiling with water completely decomposes it, and the solution on cooling deposits the pure anhydride $C_{10}H_8O_4$. The acid is readily soluble in hot and cold alcohol, ether, and chloroform, but only sparingly in cold benzene and light petroleum. The dry substance may be heated at 100° for some time without undergoing much decomposition, but at a temperature of 120—130° it rapidly liquefies, and is soon completely converted into its anhydride. The acid dissolves very readily in concentrated solutions of hydrogen iodide or bromide, and on gently warming it is very rapidly converted into the anhydride, which, on the addition of water, separates in plates. The acid does not combine with hydroxylamine.

The dissociation constant for the electric conductivity of the acid $C_{10}H_{10}O_5$ at different concentrations was kindly determined by Dr. Walker and found to be $K = 0{\cdot}0081$. The acid is therefore stronger than benzoic acid, and about as strong as metahydroxybenzoic acid or orthomethoxybenzoic acid.

The solution of the pure substance in dilute sodium carbonate does not decolorise potassium permanganate except after long standing, a proof that the acid is not unsaturated (compare Baeyer, *Annalen*, **245**, 146). An aqueous solution of the acid is not precipitated by lead acetate, neither does it reduce ammoniacal nitrate of silver or Fehling's solution.

Fusion of the Acid $C_{10}H_{10}O_5$ *with Potash.*—1 gram of the pure substance was dissolved in concentrated aqueous potassium hydrate, the solution evaporated in a silver basin, and heated at 180° for about 10 minutes. Water was added, the clear solution acidified, and extracted four times with ether. The ethereal solution, on evaporation, deposited a small quantity of a light brown oil, which was very soluble in water; the solution gave with ferric chloride a deep green coloration and other reactions characteristic of a catechol derivative.

Oxidation of the Acid $C_{10}H_{10}O_5$.—A large number of experiments were made on the action of oxidising agents on this acid, as it appeared probable that in this way some clue to its constitution might be obtained. 2 grams of the pure substance was dissolved in dilute

sodium hydrate, and a very dilute solution of potassium permanganate (5 grams) run in in the cold. Oxidation took place at once with formation of a brown solution, but no hydrated oxide of manganese was precipitated until the liquid was boiled. The product was filtered, the clear solution evaporated to a small bulk, and acidified with dilute hydrochloric acid. A white, crystalline precipitate separated at once, which weighed 1·2 grams, and consisted of the pure acid $C_{10}H_{10}O_5$.

Analysis:—

0·1678 gram substance gave 0·0740 gram H_2O and 0·3514 gram CO_2.

	Theory. $C_{10}H_{10}O_5$.	Found.
C	57·14 per cent.	57·11 per cent.
H	4·77 „	4·89 „

The filtrate from these crystals was repeatedly extracted with ether, and on evaporating the ethereal solution a colourless oil remained which solidified on standing; on recrystallisation from water, it melted at 126°, and consisted of the anhydride $C_{10}H_8O_4$. No other product could be isolated. It is probable, therefore, that the oxidation completely destroys part of the substance, leaving the remainder untouched. This experiment was repeated several times under the most varied conditions, but always with the same result.

Negative results were also obtained on using dilute nitric acid, iodine and sodium carbonate, and chromic acid as oxidisers.

Salts of Hydroxyethylpiperonylcarboxylic Acid.

In order, in the first place, to determine the basicity of this acid, the pure anhydride was dissolved in excess of standard potassium hydrate solution, a trace of phenolphthaleïn added, and the solution neutralised with standard sulphuric acid:—

0·63 gram of substance required for neutralisation 33·8 c.c. of standard potassium hydrate solution, containing in 1 c.c. 0·005461 gram KOH; the amount required for neutralisation was therefore 0·185 gram KOH. This proves that the acid is monobasic, as on this assumption 0·184 gram KOH would be required for neutralisation.

Silver Salt, $C_{10}H_9O_5Ag$.—The preparation of a sample of this salt pure enough for analysis was attended with considerable difficulty. The preparation which gave the best results was obtained by dissolving the acid in a slight excess of ammonia, removing the excess by allowing the solution to stand over sulphuric acid until nearly

neutral, and then precipitating the slightly alkaline solution by nitrate of silver. The white, crystalline precipitate was well washed, and dried on a porous plate over sulphuric acid under reduced pressure.

Analysis:—

0·2651 gram substance gave 0·0720 gram H_2O, 0·3730 gram CO_2, and 0·0894 gram Ag.

	Theory. $C_{10}H_9O_5Ag$.	Found.
C	37·85 per cent.	38·34 per cent.
H	2·84 „	3·02 „
Ag	34·07 „	33·72 „

Other analyses gave similar results, the carbon and hydrogen determinations being always too high, the silver determination too low; in one or two cases, the silver was found as low as 30—31 per cent. The explanation of this is that the silver salt always contained small quantities of the anhydride $C_{10}H_8O_4$, and it is extremely probable that perfectly accurate numbers might be obtained by dissolving the acid in dilute potassium hydrate solution, neutralising with dilute nitric acid, and then precipitating with silver nitrate (compare Salts of Berberilic Acid, p. 1049). The silver salt is crystalline, and moderately soluble in hot water.

A moderately dilute solution of the ammonium salt showed the following behaviour with reagents:—

Copper Sulphate.—A dark green precipitate readily soluble in hot water.

Lead Acetate.—A white precipitate readily soluble in hot water.

Zinc Sulphate.—
Cadmium Chloride.—
Barium Chloride.—
} No precipitate.

The *potassium salt* may be obtained in long needles by dissolving the anhydride $C_{10}H_8O_4$ in a warm and strong solution of pure potassium hydrate, and allowing the clear solution to cool slowly.

The *methylamine salt* was prepared by dissolving the pure acid in a slight excess of an aqueous solution of methylamine, and allowing the solution to evaporate over sulphuric acid under reduced pressure. A thick, oily residue was obtained which slowly crystallised. This salt was prepared, because it was thought very probable that on dry distillation it would yield oxyhydrastinine and water, thus:—

$$CH_2{<}^{O}_{O}{>}C_6H_2{<}^{COO\cdot NH_3\cdot CH_3}_{CH_2\cdot CH_2\cdot OH} = CH_2{<}^{O}_{O}{>}C_6H_2{<}^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2} + 2H_2O,$$

a decomposition which would be of considerable theoretical interest. The salt was rapidly distilled from a small retort, quantities of steam and methylamine were evolved, and an oily distillate was obtained, which, on cooling, solidified to a hard cake of crystals. These, after recrystallisation from water, melted at 126°, and showed all the properties of the anhydride $C_{10}H_8O_4$, and no trace of oxyhydrastinine could be isolated.

ω-Hydroxyethylbromopiperonylcarboxylic acid,

$$C_{10}H_9BrO_5 = CHBr<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2\cdot OH\end{matrix}\ (?),$$

and its Anhydride, $C_{10}H_7BrO_4 = CHBr<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix}\ (?).$

The bromination of the anhydride $C_{10}H_8O_4$ is readily accomplished by exposing the finely-divided substance to bromine vapour under a bell jar, in the presence of direct sunlight. After standing for three days, a dark-brown semi-solid mass is obtained, which is freed from excess of bromine by exposure to a current of air, and then ground up with a little alcohol in a mortar. This treatment removes a quantity of dark-coloured impurity, leaving behind an almost colourless powder, which, after repeated recrystallisation from alcohol, is readily obtained pure in the form of colourless needles. For analysis, the substance was dried at 110° :—

0·2015 gram substance gave 0·0480 gram H_2O and 0·3248 gram CO_2.

0·2340 gram substance, heated in a sealed tube with nitric acid and nitrate of silver at 120—130° for four hours, gave 0·1638 gram AgBr.

	Theory. $C_{10}H_7BrO_4$.	Found.
C	44·28 per cent.	43·96 per cent.
H	2·47 „	2·64 „
Br.....	29·52 „	29·76 „

This new substance melts at 146—147°. It is readily soluble in hot benzene and hot alcohol, excessively soluble in chloroform, moderately so in carbon bisulphide, but only sparingly in light petroleum or water. It crystallises from alcohol in wooly needles, from carbon bisulphide in hard balls of needles. It is insoluble in alkalis and alkaline carbonates in the cold, and is only very slowly decomposed even on long boiling with sodium hydrate solution. Alcoholic potash, on the other hand, readily dissolves it with forma-

tion of the potassium salt of ω-hydroxyethylbromopiperonylcarboxylic acid, thus :—

$$CHBr<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix} + KOH =$$

$$CHBr<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOK\\CH_2\cdot CH_2\cdot OH\end{matrix}$$

2 grams of the pure compound $C_{10}H_7BrO_4$ was mixed with a little methyl alcohol, a considerable excess of methyl alcoholic potash added, and the whole heated to boiling. In a short time the crystals had entirely dissolved, but almost immediately afterwards a quantity of a white, crystalline substance separated, which was the potassium salt of the new acid $C_{10}H_9BrO_5$. Sufficient hot water was added to bring this again into solution, the liquid boiled to expel the methyl alcohol, and the well-cooled solution acidified with dilute hydrochloric acid. The very voluminous amorphous precipitate thus produced was collected, washed with water, dried on a porous plate, and dissolved in a little boiling 80 per cent. methyl alcohol. This solution on cooling deposited the new compound in the form of beautiful, colourless needles, which, after washing with methyl alcohol and drying first on a porous plate and then for a short time at 80°, gave the following numbers on analysis :—

0·1654 gram substance gave 0·0480 gram H_2O and 0·2505 gram CO_2.

	Theory. $C_{10}H_9BrO_5$.	Found.
C	41·52 per cent.	41·31 per cent.
H	3·11 „	3·27 „

This acid melts at 146—147°, and is at the same time decomposed into water and the anhydride $C_{10}H_7BrO_4$. It is readily soluble in hot alcohol, but is almost completely deposited on cooling ; it is sparingly soluble in benzene, light petroleum, chloroform, and hot water, almost insoluble in cold water. It dissolves very readily in fuming hydriodic acid, but not in fuming hydrochloric acid. It dissolves with great ease in alkalis and alkaline carbonates, but no salts have been analysed. The potassium salt crystallises from water, in which it is not very soluble, in long, slender needles. The acid $C_{10}H_9BrO_5$ dissolves readily in warm concentrated nitric acid, forming a deep-red solution, which, on warming, gets darker and darker until ultimately oxidation sets in. Water precipitates from this solution a salmon-coloured mass, which crystallises from alcohol, in which it is sparingly soluble, in slender needles; these turn dark at 250° without melting. This substance contains both nitrogen and bromine : it is insoluble in cold potassium hydrate, but on warming it dissolves forming an intense

reddish-violet solution. This compound is most probably *ω-hydroxyethylbromonitropiperonylcarboxylic anhydride*, $C_{10}H_6Br(NO_2)O_4$.

ω-Hydroxyethylnitropiperonylcarboxylic Anhydride,

$$C_{10}H_7O_4(NO_2) = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H(NO_2)<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix}.$$

The anhydride $C_{10}H_8O_4$ dissolves readily in concentrated nitric acid, forming a deep reddish-brown solution; on the addition of water, a yellow, crystalline precipitate is obtained, which consists of the almost pure nitro-compound. The precipitate was collected, washed with water, dissolved in boiling water, and filtered from a small quantity of insoluble matter. The clear solution, after a time, deposited long, thin, yellowish needles, which, after well washing and drying at 100°, gave the following numbers on analysis:—

0·1524 gram substance gave 0·0430 gram H_2O and 0·2840 gram CO_2.

0·1830 gram substance gave 9·6 c.c. N; $t = 18°$; bar. = 759 mm.

	Theory. $C_{10}H_7O_4NO_2$.	Found.
C	50·63 per cent.	50·82 per cent.
H	2·95 „	3·13 „
N	5·90 „	6·17 „

This nitro-derivative melts at 197°. It is readily soluble in hot water and alcohol, but only sparingly in these liquids in the cold. It is also sparingly soluble in benzene and light petroleum. It is insoluble in sodium hydrate solution in the cold, but on warming it dissolves, forming a deep yellow solution, which rapidly darkens, becoming dark brown and ultimately of a beautiful violet colour. Acids destroy this colour, but it reappears on the addition of an alkali.

ω-Hydroxyethylcatecholcarboxylic Anhydride,

$$C_9H_8O_4 = (OH)_2C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix}.$$

When heated in sealed tubes with dilute hydrochloric, hydrobromic, or hydriodic acid at 180°, or with distilled water at 210°, *ω*-hydroxyethylpiperonylcarboxylic anhydride, $C_{10}H_8O_4$, is decomposed, a deposit of carbon being formed on the sides of the tube. In all these cases ether extracts from the filtered solution a sticky substance; this dissolves readily in water and gives with ferric chloride an intense green coloration, which becomes violet and, finally, red on the addition of sodium hydrogen carbonate. This behaviour shows conclusively that the anhydride $C_{10}H_8O_4$ must be a derivative of catechol, in which

the hydroxyl hydrogens are substituted, probably by two methyl groups or by the methylene group.

In order to determine whether methoxy-groups were present in the molecule, 0·2345 gram of the substance was introduced into a Zeisel's apparatus (*Monatsh.*, **6**, 995) and heated with hydriodic acid, but, even after two hours, no trace of methyl iodide had been evolved, as shown by the fact that the alcoholic silver nitrate employed remained perfectly clear throughout. This proves that the substance $C_{10}H_8O_4$ contains no methoxy-group.

As all attempts to isolate the product of the reaction from the residual hydriodic acid solution gave unsatisfactory results, a large number of experiments on the action of hydrobromic and hydrochloric acids on the anhydride $C_{10}H_8O_4$ were made, the strength of the acids and the temperature of the decomposition being varied in each case. It was soon found that the product of the reaction could only be satisfactorily isolated when the strength of the acid (hydrochloric acid gave the best results) and the range of the temperature were kept within narrow limits. By carefully observing the following conditions excellent results were obtained:—

1 gram of the anhydride $C_{10}H_8O_4$ was ground up, mixed with 40 c.c. of water, 10 c.c. of ordinary concentrated hydrochloric acid (sp. gr. 1·168) added, and the mixture heated in a sealed tube for five hours at 170—175°.

The tube, which on cooling opened without pressure, was found to be filled with light flocks of charcoal, most of which adhered firmly to the under side of the tube. These were filtered off and the resulting almost colourless solution extracted six times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited an almost colourless, crystalline residue. This was dissolved in a small quantity of hot water, the solution filtered into a glass dish, and allowed to evaporate to a small bulk over sulphuric acid under reduced pressure at the ordinary temperature. After standing for some time, the new substance separated in peculiar, hard, nodular masses, which were collected, washed with a little water, and dried at 100°.

The analyses gave the following results:—

I. 0·1618 gram substance gave 0·0686 gram H_2O and 0·3542 gram CO_2.

II. 0·1316 gram substance gave 0·0554 gram H_2O and 0·2892 gram CO_2.

	Theory. $C_9H_8O_4$.	Found. I.	Found. II.
C	60·00 per cent.	59·71	59·93 per cent.
H	4·44 „	4·71	4·67 „
O	35·55 „	35·58	35·40 „

This substance is formed from the anhydride $C_{10}H_8O_4$ by the simple separation of carbon, thus:—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\ |\\CH_2\cdot CH_2\end{matrix} = C + \begin{matrix}HO\\HO\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\ |\\CH_2\cdot CH_2\end{matrix}.$$

When heated in a capillary tube, it becomes soft at 210° and melts, not very sharply, at 220—225°. It is readily soluble in hot and cold water, and much more so than either of the substances $C_{10}H_8O_4$ or $C_{10}H_{10}O_5$; it is moderately soluble in methyl and ethyl alcohols, sparingly in benzene and chloroform. It dissolves readily in cold dilute caustic potash solution, forming a yellowish-coloured liquid. Its aqueous solution, with acetate of lead, gives a white, amorphous precipitate, soluble in much hot water; it also reduces ammoniacal nitrate of silver solution and Fehling's solution very rapidly in the cold. A drop of ferric chloride solution added to the aqueous solution produces at once an intense green coloration, which, on the careful addition of sodium hydrogen carbonate, gradually turns violet and finally deep red. The decomposition of the anhydride $C_{10}H_8O_4$, on heating with dilute hydrochloride acid, into $C_9H_8O_4$ and carbon is exactly similar to the change which piperonylic acid undergoes under like conditions. Fittig and Remsen (*Annalen*, **159**, 139) have shown that this acid, when heated at 170° with dilute hydrochloric acid, is converted into protocatechuic acid, with deposition of charcoal, thus:—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_3\cdot COOH = C + \begin{matrix}HO\\HO\end{matrix}>C_6H_3\cdot COOH.$$

Piperonylic acid. Protocatechuic acid.

The compound $C_{10}H_8O_4$ is, therefore, a piperonyl derivative, and the above experiment gave the first important clue as to the constitution of this substance and its derivatives.

Action of Phosphorus Pentachloride on the Anhydride $C_{10}H_8O_4$.

ω-Chlorethylpiperonylcarboxylic Acid, $C_{10}H_9ClO_4$ =

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2Cl\end{matrix}$$

In order to obtain some further clue to the constitution of the anhydride $C_{10}H_8O_4$, a very careful examination of the action of phosphorus pentachloride on this compound was undertaken.

2 grams of the pure dry substance was dissolved in 25 grams of chloroform, and then 3 grams of powdered pentachloride of phosphorus added. Scarcely any action took place in the cold, but on heating on a water-bath, considerable quantities of hydrogen chloride were evolved. The mixture, after gently boiling on a reflux apparatus

for about half an hour, was cooled, 2 grams of phosphorus pentachloride added, and the heating continued for another half hour. The product on cooling deposited a quantity of yellowish crystals, which readily dissolved again on warming. These crystals seemed to consist of the acid chloride,

$$CH_2<^{O}_{O}>C_6H_2<^{COCl}_{CH_2\cdot CH_2Cl},$$

mixed with small quantities of phosphorus pentachloride, but although several attempts were made to isolate the pure substance, no very satisfactory numbers could be obtained on analysis. That this acid chloride is contained in this product is proved by the decomposition which it undergoes on being mixed with methyl alcohol (see p. 1033).

In examining the product formed in the above reaction, the excess of chloroform was distilled off, the resulting brownish oil cautiously added to a quantity of powdered ice, and the whole allowed to stand until the phosphorus oxychloride and excess of pentachloride had been completely decomposed. The liquid was extracted three times with ether, the ethereal solution washed with water, dried over calcium chloride, and evaporated, when a thick, unpleasantly-smelling syrup was obtained which on standing solidified almost completely. The crystalline cake was well pressed to remove adhering oily matter, washed with a little 80 per cent. methyl alcohol, and dissolved in a small quantity of boiling chloroform. From this solution, the substance separated on cooling in long, thin, colourless needles, which after recrystallisation were readily obtained pure.

Analysis:—

0·1714 gram substance gave 0·0624 gram H_2O and 0·3310 gram CO_2.

0·2149 gram substance, heated in a sealed tube with nitric acid and nitrate of silver at 180° for four hours, gave 0·1315 gram AgCl.

	Theory. $C_{10}H_9O_4Cl$.	Found.
C	52·54 per cent.	52·66 per cent.
H	3·94 „	4·04 „
Cl	15·49 „	15·10 „

This substance $C_{10}H_9ClO_4$ is evidently formed from the anhydride $C_{10}H_8O_4$, as shown in the following equations:—

$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot O}_{CH_2\cdot CH_2}> + PCl_5 = CH_2<^{O}_{O}>C_6H_2<^{COCl}_{CH_2\cdot CH_2Cl} + POCl_3,$$

$$CH_2<^{O}_{O}>C_6H_2<^{COCl}_{CH_2\cdot CH_2Cl} + H_2O = CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2Cl} + HCl,$$

the acid chloride first formed being further decomposed on pouring the product into water. The substance $C_{10}H_9ClO_4$ crystallises from chloroform in long, thin, prismatic needles, which grow to a considerable length if the solution is allowed to cool slowly. It melts at 158—159° with decomposition, is readily soluble in ether, methyl and ethyl alcohols, and acetic acid, sparingly in water and cold chloroform. This latter property renders the separation of the chloride from any unchanged or regenerated anhydride $C_{10}H_8O_4$, with which the crude product is nearly always contaminated, a matter of no difficulty, as the latter is excessively soluble in chloroform.

The substance $C_{10}H_9ClO_4$ dissolves readily in alkalis and alkaline carbonates. When heated in the dry state, it decomposes at about 160°, with evolution of hydrogen chloride and formation of the anhydride $C_{10}H_8O_4$, thus :—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2Cl\end{matrix} = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH_2\cdot CH_2\end{matrix} + HCl,$$

a reaction very similar to that occurring in the formation of lactones from γ-halogen derivatives, *e.g.*, by the action of heat on γ-chlorobutyric acid (L. Henry, *Compt. rend.*, **101**, 1158—1161). When digested with alcoholic potash, the substance $C_{10}H_9ClO_4$ is readily decomposed with separation of potassium chloride. This reaction was studied in detail, because it was thought possible that an unsaturated derivative might result containing the side group $CH{:}CH_2$, thus :—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2Cl\end{matrix} + 2KOH = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOK\\CH{:}CH_2\end{matrix} + KCl + H_2O,$$

a decomposition which would be of considerable interest as determining the exact nature of the side chains in the compound $C_{10}H_8O_4$.

1 gram of the pure chloride was added to an excess of very strong alcoholic potash, and the whole boiled until the deposition of potassium chloride had ceased. The product was mixed with water, heated on a water-bath until free from alcohol, well cooled, and acidified with hydrochloric acid. The crystalline precipitate was collected, washed with water, and recrystallised from this solvent; when colourless needles were obtained which melted at 126° and showed all the properties of the anhydride $C_{10}H_8O_4$.

Analysis :—

0·1759 gram of substance gave 0·0663 gram H_2O and 0·4020 gram CO_2.

	Theory. $C_{10}H_8O_4$.	Found.
C	62·50 per cent.	62·39 per cent.
H	4·17 „	4·19 „

The regeneration of the anhydride $C_{10}H_8O_4$ in this reaction is easily accounted for by the following equation:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2Cl} + 2KOH =$$

$$CH_2<^{O}_{O}>C_6H_2<^{COOK}_{CH_2\cdot CH_2\cdot OH} + KCl + H_2O.$$

On acidifying with hydrochloric acid, the acid $C_{10}H_{10}O_5$ is precipitated, and this, on recrystallisation from water, is readily converted into its anhydride, $C_{10}H_8O_4$ (p. 1021).

As the experiments did not afford any clue to the nature of the side chains in the anhydride $C_{10}H_8O_4$, the action of methylamine on the compound $C_{10}H_9ClO_4$ was carefully studied. It seemed extremely probable that this reaction should lead to a synthesis of oxhydrastinine, thus:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2Cl} + 2CH_3\cdot NH_2 =$$

$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2}> + CH_3\cdot NH_2,HCl + H_2O.$$

Oxyhydrastinine.

a synthesis which would at once prove the constitution of the anhydride $C_{10}H_8O_4$. This experiment was repeated several times under the most varied conditions, and great care was taken to exclude every trace of water, but in all cases an almost quantitative yield of the anhydride $C_{10}H_8O_4$ was obtained, the methylamine acting obviously much in the same way as alcoholic potash.

Similar results were obtained in experiments on the reduction of the chloride $C_{10}H_9ClO_4$ with zinc and acetic acid, and other reducing agents; the anhydride $C_{10}H_8O_4$ being the only product which could be isolated.

Methylic ω-Chlorethylpiperonylcarboxylate,

$$C_{11}H_{11}O_4Cl = CH_2<^{O}_{O}>C_6H_2<^{COOCH_3}_{CH_2\cdot CH_2Cl}.$$

This important substance has been prepared in considerable quantities for use in a number of synthetical experiments. It can be obtained in almost quantitative yield in the following way:—5 grams of the anhydride $C_{10}H_8O_4$ are dissolved in 30 grams of chloroform,

10 grams of powdered pentachloride of phosphorus added, and the mixture heated to boiling for half an hour in a reflux apparatus. The condenser is then removed, the chloroform boiled away, and the residual thick, oily mass, while still warm, poured in a thin stream into a considerable quantity of pure absolute methyl alcohol, the whole being well cooled during the operation. As soon as the very energetic reaction, which at once sets in, has subsided, the bulk of the methyl alcohol is distilled off, and the residue poured into cold water. The white, flocculent precipitate which separates is collected, well washed with water, dried on a porous plate, extracted with small quantities of boiling methyl alcohol, and the solution filtered from a small quantity of a white, insoluble substance. After distilling off the excess of methyl alcohol, the hot solution deposits, on cooling, long, beautiful, colourless needles of the nearly pure methyl salt. These were collected, recrystallised from methyl alcohol, and analysed with the following results:—

I. 0·1580 gram substance gave 0·0687 gram H_2O and 0·3144 gram CO_2.

0·1530 gram substance gave 0·2570 gram AgCl.

II. 0·1517 gram substance gave 0·0662 gram H_2O and 0·3030 gram CO_2.

	Theory. $C_{11}H_{11}O_4Cl$.	Found. I.	Found. II.
C	54·45 per cent.	54·27	54·47 per cent.
H	4·54 „	4·82	4·84 „
Cl	14·61 „	14·79	— „

This methyl salt is obviously produced by the action of methyl alcohol on the acid chloride produced by the interaction of the phosphorus pentachloride and the anhydride $C_{10}H_8O_4$, thus:—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COCl\\CH_2\cdot CH_2Cl\end{matrix} + CH_3\cdot OH =$$

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOCH_3\\CH_2\cdot CH_2Cl\end{matrix} + HCl.$$

The pure substance melts at 82—83°. It is readily soluble in benzene, light petroleum, methyl alcohol, and chloroform, sparingly in water, but excessively soluble in ether. It crystallises best from 80 per cent. methyl alcohol. It is readily hydrolysed by boiling with alcoholic potash, with regeneration of the acid $C_{10}H_{10}O_5$.

This methyl salt is of considerable value from a theoretical point of view, as when heated with primary amines it yields amido-derivatives, which, on hydrolysis with alcoholic potash, are converted into derivatives of isoquinoline, thus:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOCH_3}_{CH_2\cdot CH_2Cl} + 2RNH_2 =$$
$$CH_2<^{O}_{O}>C_6H_2<^{COOCH_3}_{CH_2\cdot CH_2\cdot NHR} + NH_2R,HCl.$$

$$CH_2<^{O}_{O}>C_6H_2<^{COOCH_3}_{CH_2\cdot CH_2\cdot NHR} =$$
$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot NR}_{CH_2\cdot CH_2} + CH_3\cdot OH.$$

Thus, when heated with methylamine, oxyhydrastine is formed; a synthesis which at once proves the constitution of the anhydride $C_{10}H_8O_4$, and indirectly that of the substance $C_{10}H_9NO_3$ (see Introduction, p. 998). Similarly constituted isoquinoline derivatives have also been obtained by heating the methyl salt with aniline and with ethylamine, as will be described in the subsequent chapters.

Oxyhydrastinine, $C_{11}H_{11}NO_3 = CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2}$.

This substance, which has been proved to have the constitution assigned to it above, was first obtained by Freund and Will (*Ber.*, **20**, 2401; compare Freund and Lachmann, *Ber.*, **22**, 2323) by the action of potassium hydrate on hydrastinine, thus:—

$$2CH_2<^{O}_{O}>C_6H_2<^{COH}_{CH_2\cdot CH_2\cdot NH\cdot CH_3} + H_2O =$$

Hydrastinine.

$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2} +$$

Oxyhydrastinine.

$$CH_2<^{O}_{O}>C_6H_2<^{CH_2\cdot OH}_{CH_2\cdot CH_2\cdot NH\cdot CH_3} + H_2O.$$

Hydrohydrastinine.

It may be obtained synthetically from methylic ω-chlorethylpiperonylcarboxylate by the action of methylamine in the following way:—

2 grams of the methylic salt were heated in a sealed tube with a strong alcoholic solution of methylamine (prepared by passing *dry* methylamine into absolute alcohol) for three hours at 100—120°, and then for three hours at 120—130°. The clear, almost colourless product was freed from excess of methylamine and from alcohol by evaporation, and the residue boiled for one hour with a strong alcoholic solution of potassium hydrate. Water was added, the alcohol driven off on a water-bath, and the product, which contained

oily drops, allowed to stand for 48 hours in a cool place; at the end of this time it was found that the oily drops had completely solidified. The hard, crystalline masses were collected, washed with water, freed from a trace of oily impurity by spreading on a porous plate, and purified by recrystallisation from dilute alcohol. In this way beautiful, colourless, glistening plates were obtained which, after drying first over sulphuric acid under reduced pressure and then at 80°, gave the following numbers on analysis:—

0·1562 gram substance gave 0·0798 gram H_2O and 0·3690 gram CO_2.

0·1366 gram substance gave 8·3 c.c. N; $t = 20°$; bar. = 740 mm.

	Theory. $C_{11}H_{11}NO_3$.	Found.
C.....	64·39 per cent.	64·43 per cent.
H.....	5·36 „	5·67 „
N.....	6·83 „	6·80 „

It melts at 97—98°, and is identical in all its properties with oxyhydrastinine.

The yield of this substance, obtained in the above reaction, is almost theoretical; but a very small quantity of an acid is also produced at the same time, which remains dissolved in the strong alkali, and may be extracted by ether after acidifying with hydrochloric acid. It was not further examined.

The synthesis of oxyhydrastinine from methylic ω-chlorethylpiperonylcarboxylate is readily understood by substituting CH_3 for R in the general equation, p. 1034.

Ethylamidoethylpiperonylcarboxylic Anhydride,

$$C_{12}H_{13}NO_3 = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot N\cdot C_2H_5\\ |\\CH_2\cdot CH_2\end{matrix}.$$

This may be prepared by the action of an alcoholic solution of ethylamine on methylic ω-chlorethylpiperonylcarboxylate, the method being similar to that employed in the synthesis of oxyhydrastinine. The product of the reaction, after boiling with alcoholic potash as described above, was a thick oil which, even on long standing, did not solidify. It was extracted from the alkaline liquors with pure ether, the ethereal solution washed, dried over calcium chloride, carefully filtered, and the ether evaporated. The residual, almost colourless oil was completely freed from moisture and ether by standing over sulphuric acid under reduced pressure, and then analysed with the following result:—

0·2264 gram substance gave 13·7 c.c. N; $t = 18°$; bar. = 746 mm.

	Theory. $C_{12}H_{13}NO_3$.	Found.
N	6·39 per cent.	6·80 per cent.

Ethylamidopiperonylcarboxylic anhydride is a colourless oil which, when heated in small quantities, distils almost undecomposed. The yield obtained in the above synthesis is almost quantitative, and the crude product evidently nearly pure.

Phenylamidoethylpiperonylcarboxylic Anhydride,

$$C_{16}H_{13}NO_3 = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot N\cdot C_6H_5\\ |\\CH_2\cdot CH_2\end{matrix}.$$

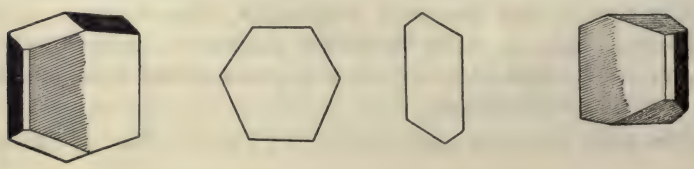
In preparing this substance, pure methylic ω-chlorethylpiperonylcarboxylate was dissolved in alcohol, excess of aniline added, and the mixture boiled in a reflux apparatus for half an hour. The alcohol was distilled off, the oily residue heated at 170—180° for half an hour, and the resulting dark-coloured mass hydrolysed by boiling with alcoholic potash. The product was mixed with water, the alcohol and excess of aniline driven off by distillation in a current of steam, and the residual liquid, which contained a dark-coloured, resinous substance, digested for five minutes with very dilute hydrochloric acid. The solid substance which separated was collected, washed with water, and ground up in a mortar with a little 80 per cent. alcohol. In this way a quantity of a dark, resinous substance was removed, leaving a brownish, crystalline mass; this, when dissolved in boiling alcohol, was deposited in beautiful glistening, colourless prisms as the solution cooled; the separation is very much hastened by the addition of a crystal of the crude substance.

The analysis gave the following numbers:—

0·1927 gram substance gave 9·1 c.c. N; $t = 23°$; bar. = 746 mm.

	Theory. $C_{16}H_{13}NO_3$.	Found.
N.... ...	5·24 per cent.	5·22 per cent.

This substance melts at 157°. It is very soluble in hot alcohol, benzene, and xylene, sparingly in water, cold alcohol, light petroleum, and carbon bisulphide, and exceedingly soluble in chloroform. Beautiful crystals are obtained by allowing the solution in benzene to evaporate spontaneously; these have the following forms:—



Anhydroberberilic Acid,

$$C_{20}H_{17}NO_8 = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot CH_2>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2.$$

This important compound is the principal constituent of the yellow precipitate obtained by the oxidation of berberine with potassium permanganate and subsequent treatment with sulphurous anhydride, as described on p. 1011. The methods employed in the isolation and purification of this substance are given in Part I of this research (*loc. cit.*, pp. 79 and 80).

Even after repeated recrystallisation from acetic acid, anhydroberberilic acid is almost always slightly discoloured by the presence of a very small quantity of a yellowish impurity which can only be completely removed with difficulty. On several occasions a beautifully pure product has been obtained by recrystallising the crude compound, first from large quantities of alcohol and then from glacial acetic acid.

An analysis confirmed the formula previously arrived at as representing the composition of this substance :—

0·1860 gram substance gave 0·0742 gram H_2O and 0·4095 gram CO_2.

0·2248 gram substance gave 7·1 c.c. N ; $t = 16°$; bar. = 740 mm.

	Theory. $C_{20}H_{17}NO_8$.	Found.	Mean of previous analyses.
C	60·15 per cent.	60·04 per cent.	59·84 per cent.
H	4·26 ,,	4·43 ,,	4·47 ,,
N	3·51 ,,	3·53 ,,	3·54 ,,

Anhydroberberilic acid, when quite pure, is colourless, and has a most beautful, satiny lustre. It is very sparingly soluble in alkalis and alkaline carbonates in the cold, but when in a very finely-divided state (as obtained by grinding with water) it dissolves readily, even in alkaline carbonates at a temperature of 30—40°, and is reprecipitated unchanged on the addition of an acid. It therefore has acid properties, and is not a neutral substance, as was at first thought to be the case. In addition to the properties already given in Part I of this research, may be added that anhydroberberilic acid is not acted on by phenylhydrazine or by prolonged boiling with methyl iodide.

Salts of Anhydroberberilic Acid.

Very considerable difficulty was experienced in preparing salts directly derived from this acid, for the reason that when dissolved in ammonia or solutions of caustic alkalis, salts of berberilic acid (see p. 1048) are formed, thus :—

$$C_{20}H_{17}NO_8 + 2KOH = C_{20}H_{17}NO_9K_2 + H_2O.$$

It was, however, subsequently observed that the ammonium salt of berberilic acid, $C_{20}H_{17}NO_9(NH_4)_2$, on long standing over sulphuric acid in a vacuum, or much more rapidly on warming its aqueous solution, gradually gives off one-half of its ammonia, and yields the ammonium salt of anhydroberberilic acid, thus :—

$$C_{20}H_{17}NO_9(NH_4)_2 = C_{20}H_{16}NO_8(NH_4) + NH_3 + H_2O.$$

This salt, on the addition of an acid, now gives a precipitate of anhydroberberilic acid, instead of one of berberilic acid, as was the case at first.

This behaviour accounts for the fact that previously (Part I, p. 81) good numbers could not be obtained in the analysis of the silver salt prepared by precipitating a solution of the ammonium salt with silver nitrate. The analysis gave numbers lying between those required for the bibasic salt $C_{20}H_{17}NO_9Ag_2$ and those required for the monobasic salt $C_{20}H_{16}NO_8Ag$, showing that the bibasic ammonium salt used had already undergone some decomposition.

Silver Salt.—In re-examining the salts of anhydroberberilic acid, the pure substance was ground up with water to the consistency of a thin paste, rendered decidedly alkaline with ammonia, and gently warmed on a water-bath at 30—40° until the whole had dissolved. The solution was then placed in a dish over sulphuric acid in a vacuum, and allowed to evaporate almost to dryness. The gelatinous residue was dissolved in water with the aid of a drop of ammonia, heated at 60° on a water-bath for two or three hours, filtered, and the solution precipitated by silver nitrate in three fractions, at a temperature of about 40°, a preliminary precipitate of a small quantity being discarded. By this method the silver salt is obtained as a white, granular powder which is readily washed, whereas, if the precipitation takes place in the cold, the salt is gelatinous. The middle fraction was well washed with cold water, dried on a porous plate, first over sulphuric acid in a vacuum and then at 60°, and analysed with the following results :—

I. 0·1514 gram substance gave 0·0483 gram H_2O, 0·2620 gram CO_2, and 0·0328 gram Ag.

II. 0·2684 gram substance gave 0·0560 gram Ag.

	Theory. $C_{20}H_{16}NO_8Ag$.	Found. I.	Found. II.	
C.....	47·43 per cent.	47·20	—	per cent.
H.....	3·16 „	3·55	—	„
Ag.....	21·34 „	21·66	20·86	„

This silver salt is sparingly soluble in water, and very stable; even prolonged heating at 100° scarcely decomposes it; for ordinary purposes it may therefore be dried at 100°.

Copper Salt, $(C_{20}H_{16}NO_8)_2Cu + 2H_2O$.—This salt was obtained as a brilliant, light-blue precipitate by the addition of a solution of copper sulphate to the solution of the ammonium salt. It was well washed with water and dried over sulphuric acid in a vacuum.

Analysis:—

0·2632 gram substance, heated at 100° till the weight became constant, lost 0·0104 gram = 3·99 per cent.

$(C_{20}H_{16}NO_8)_2Cu + 2H_2O$ contains 4·02 per cent. Aq.

The dry substance (0·2528 gram), on ignition in a current of air, left 0·0247 gram CuO.

	Theory. $(C_{20}H_{16}NO_8)_2Cu$.	Found.
Cu.....	7·36 per cent.	7·79 per cent.

A dilute neutral solution of the ammonium salt shows the following behaviour with reagents:—

Cadmium Chloride.—A white, gelatinous precipitate.

Lead Acetate.—A white, gelatinous precipitate, somewhat soluble in hot water.

Barium and Calcium Chlorides.—No precipitates.

Methyl Salt of Anhydroberberilic Acid,

$$C_{20}H_{16}NO_8(CH_3) = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!N\cdot CH_2\cdot CH_2\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.\quad COOCH_3$$

In order to be certain as to the basicity of anhydroberberilic acid, it was thought necessary to prepare some crystalline salt which could be readily purified, and from which trustworthy numbers could be obtained. As the metallic salts did not crystallise, and for this reason gave only imperfect numbers on analysis, attention was next directed to the preparation of a *methyl salt*. This salt is readily prepared by the action of methyl iodide on the silver salt, $C_{20}H_{16}NO_8Ag$. 2 grams of the pure dry silver salt was mixed with 20 c.c. of pure ether, a large excess of methyl iodide (5—10 grams) added, and the whole heated to boiling in a flask connected with a reflux apparatus. As soon as the decomposition was complete, the ether and excess of methyl iodide were distilled off, and the residue extracted three or four times with boiling absolute alcohol. The filtered extract, on evaporation, deposited an almost solid cake of the crude methyl salt; this was purified by spreading on a porous plate and subsequent

recrystallisation, twice from alcohol and once from acetic acid. The beautifully white glistening crystalline powder thus obtained was dried at 100°, and analysed with the following results:—

I. 0·1352 gram substance gave 0·0601 gram H_2O and 0·3016 gram CO_2.
0·1783 gram substance gave 5·2 c.c. N; $t = 14°$; bar. = 740 mm.

II. 0·1670 gram substance gave 0·0710 gram H_2O and 0·3720 gram CO_2.

III. 0·1724 gram substance gave 0·0734 gram H_2O and 0·3844 gram CO_2.

	Theory. $C_{20}H_{16}(CH_3)NO_8$.	Found. I.	II.	III.	
C.....	61·01	60·84	60·75	60·81	per cent.
H.....	4·60	4·93	4·72	4·73	„
N.....	3·39	3·33	—	—	„

This methyl salt melts at 178—179°. In a finely-divided condition it is moderately soluble in carbon bisulphide, boiling benzene, and alcohol, but the crystals are only very sparingly soluble in these solvents. It crystallises best from acetic acid, being deposited as a fine, crystalline powder, which, when examined under the microscope, is seen to consist of four-sided plates with bevelled edges. This methyl salt is readily hydrolysed by boiling with hydrochloric acid or alcoholic potash. In order to make sure that it was in reality a methyl salt, and that the CH_3 group was not attached to the nitrogen atom in the molecule $C_{20}H_{17}NO_8$, the number of methoxy-groups which it contained was determined by Zeisel's method (*Monatsh.*, **6**, 995).

0·3016 gram substance, when heated with fuming hydriodic acid (sp. gr. 1·96), and the resulting methyl iodide passed into an alcoholic solution of silver nitrate, gave 0·4982 gram AgI.

	Theory for $3(OCH_3)$ groups in $C_{20}H_{16}(CH_3)NO_8$.	Found.
(CH_3O)	22·52 per cent.	21·91 per cent.

Three OCH_3 groups are therefore contained in this methyl salt, two from the original berberine molecule, and one in the form of $COOCH_3$; this substance is therefore the true methyl salt of anhydroberberilic acid.

Acetylanhydroberberilic Acid,

$$C_{22}H_{19}NO_9 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!\!>\!N\!-\!CH_2\!-\!CH_2\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.$$

Acetic anhydride reacts readily with anhydroberberilic acid with formation of an acetyl derivative, thus:—

$$C_{20}H_{17}NO_8 + \begin{matrix}CH_3\cdot CO\\CH_3\cdot CO\end{matrix}\!>\!O = C_{22}H_{19}NO_9 + CH_3\cdot COOH.$$

In preparing this acetyl derivative, 2 grams of pure anhydroberberilic acid was mixed with 30 grams of acetic anhydride, and the mixture heated to boiling in a flask connected with a reflux apparatus for about three hours. The resulting brown solution, which was strongly fluorescent, was evaporated to a small bulk and allowed to stand for 12 hours. The crystals which separated were collected, washed with a little acetic anhydride, and recrystallised from this solvent. The acetyl derivative was thus obtained pure in hard, glistening, slightly yellowish prisms, which, after drying at 105° for two hours, gave the following results on analysis:—

0·1665 gram substance gave 0·0690 gram H_2O and 0·3644 gram CO_2.

0·3108 gram substance gave 9·4 c.c. N; $t = 8°$; bar. = 745 mm.

	Theory. $C_{22}H_{19}NO_9$.	Found.
C	59·82 per cent.	59·69 per cent.
H	4·28 ,,	4·60 ,,
N	3·17 ,,	3·51 ,,

Acetylanhydroberberilic acid melts at 139—140°, and at a higher temperature it decomposes with formation of an oil which smells strongly of acetic anhydride. It is very readily soluble in acetic acid, moderately in boiling alcohol, sparingly in boiling benzene and xylene, and almost insoluble in bisulphide of carbon and light petroleum. It crystallises from boiling xylene in peculiarly striated, needle-shaped crystals. The acid is very readily hydrolysed, boiling with water for a short time being sufficient to ensure complete decomposition into anhydroberberilic acid and acetic acid:—

$$C_{22}H_{19}NO_9 + H_2O = C_{20}H_{17}NO_8 + CH_3\cdot COOH.$$

The composition of the acetyl derivative may be accurately controlled by determining the amounts of these products produced on hydrolysis.

4·0610 grams of the pure substance was finely powdered and

boiled in a flask connected with a reflux apparatus with 200 c.c. of 5 per cent. sulphuric acid. In a short time, complete hydrolysis had taken place with separation of colourless, flocculent masses of anhydroberberilic acid. These were collected on a filter, washed with water, and the yellow filtrate distilled in a current of steam until the distillate no longer showed any acid reaction. The acid liquid required for neutralisation 93 c.c. of standard solution of potassium hydrate (1 c.c. = 0·00598 gram of acetic acid).

This corresponds with 0·5561 gram of acetic acid = 13·7 per cent. According to the above equation, $C_{22}H_{19}NO_9$ gives 13·6 per cent.

The anhydroberberilic acid produced in this hydrolysis was very thoroughly washed with water until quite free from sulphuric acid, dried first on a plate and then at 100° until constant. It then weighed 3·688 grams = 90·8 per cent., whereas, according to the above equation, 90·5 per cent. should be produced.

These facts leave scarcely any doubt that the acetyl derivative is in reality a mixed anhydride of acetic and anhydroberberilic acids, and as such it has been represented at the head of this section. This accounts for the readiness with which it is decomposed into acetic and anhydroberberilic acids in contact with water.

Anhydroberberilic Chloride,

$$C_{20}H_{16}NClO_7 = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>N\cdot CH_2\cdot CH_2>C_6H_2<\begin{matrix}COCl\\O\end{matrix}>CH_2.$$

The action of phosphorus pentachloride on anhydroberberilic acid seems to be complicated, and the results obtained vary considerably with the quantity of the reagent employed and the subsequent treatment of the product.

Experiment I.—3 grams of pure anhydroberberilic acid was mixed with 50 grams of chloroform, and 6 grams of powdered phosphorus pentachloride added. As no action seemed to take place in the cold, the mixture was heated to boiling for half an hour; 2 grams more pentachloride added, and the heating continued for another half-hour. The residual light-brown liquid, which, on cooling, deposited a quantity of crystals, was, while still hot, transferred to a dish and freed from phosphorus oxychloride and excess of chloroform by heating on a water-bath. The yellow, crystalline residue was powdered, dissolved in boiling benzene, and the filtered solution allowed to stand 24 hours. In this way a considerable crop of garnet-coloured crystals was obtained, which, after repeated recrystallisation from benzene, gave the following numbers on analysis:—

0·1674 gram substance gave 0·0584 gram H_2O and 0·3540 gram CO_2.

0·3962 gram substance, heated with nitric acid and silver nitrate in a sealed tube at 180° for four hours, gave 0·1410 gram AgCl.

0·2984 gram substance gave 8·8 c.c. nitrogen; $t = 17°$; bar = 736 mm.

	Theory. $C_{20}H_{16}NClO_7$.	Found.
C	57·49 per cent.	57·70 per cent.
H	3·83 „	3·87 „
N	3·35 „	3·32 „
Cl	8·50 „	8·74 „

This substance is the chloride of anhydroberberilic acid; its formation in the above reaction is represented by the equation

$$C_{20}H_{17}NO_8 + PCl_5 = C_{20}H_{16}NClO_7 + HCl + POCl_3.$$

This chloride melts at 167°, and is sparingly soluble in cold benzene, alcohol, and acetic acid. It crystallises from benzene in hard, thick, almost colourless prisms. It is practically insoluble in water, and for this reason is only very slowly acted on by this solvent. If, however, the powdered chloride is boiled with 80 per cent. acetic acid, it gradually dissolves, and, on cooling, anhydroberberilic acid crystallises out, thus:—

$$C_{20}H_{16}NClO_7 + H_2O = C_{20}H_{17}NO_8 + HCl.$$

The yield of crystalline chloride obtained in the above method of preparation is about 70 per cent. of the theoretical. A small quantity remains behind in the benzene mother liquors; by concentrating the solution, this may be recovered as a dark-coloured, crystalline mass, which is, however, difficult to purify.

Experiment II.—2 grams of anhydroberberilic acid, 12 grams of phosphorus oxychloride, and 6 grams of phosphorus pentachloride were mixed together and heated on a water-bath. In a short time the whole of the anhydro-acid dissolved, hydrogen chloride being liberated in abundance. After heating for an hour, 3 grams of phosphorus pentachloride was added, and the heating continued for another hour. The product, which, on cooling, solidified to a mass of crystals, was melted and poured, in a thin stream, into much water, the whole being kept as cool as possible during the operation. As soon as the energetic reaction, which at once sets in, had subsided, the brick-red precipitate which separated was collected, washed well, dried on a porous plate, and extracted with boiling alcohol. The greater part dissolved, leaving, however, a slight residue of regenerated anhydroberberilic acid. The alcoholic solution was evaporated to a small bulk and allowed to stand, when a brown, crystalline

powder was obtained, which, after boiling in alcoholic solution with freshly ignited animal charcoal, and adding a little water, deposited an almost colourless, semi-crystalline precipitate. This was dissolved in alcohol, mixed with an equal bulk of water, and the solution allowed to stand exposed to the air. In a short time, crystalline crusts formed on the bottom of the dish, which, after well washing with dilute alcohol and drying over sulphuric acid in a vacuum, melted at 180—182°, and showed all the properties of berberilic acid (p. 1048).

The analysis gave confirmatory results :—

0·1439 gram substance gave 0·0619 gram H_2O and 0·3039 gram CO_2.

0·2059 gram substance gave 5·8 c.c. nitrogen; $t = 17°$; bar. = 745 mm.

	Theory. $C_{20}H_{19}NO_9$.	Found.
C	57·55 per cent.	57·59 per cent.
H	4·55 ,,	4·70 ,,
N	3·36 ,,	3·20 ,,

As anhydroberberilic acid is not attacked by dilute hydrochloric acid in the cold, it seems that under the above conditions phosphorus pentachloride converts anhydroberberilic acid into the chloride of berberilic acid, which, when mixed with water is decomposed with formation of berberilic acid, thus :—

$$C_{20}H_{17}NO_8 + PCl_5 = C_{20}H_{17}NO_7Cl_2 + POCl_3,$$
$$C_{20}H_{17}NO_7Cl_2 + 2H_2O = C_{20}H_{19}NO_9 + 2HCl.$$

Experiment III.—3 grams of anhydroberberilic acid were mixed with 40 grams of chloroform, 6 grams of phosphorus pentachloride added, and the mixture heated to boiling in a reflux apparatus for half an hour. The chloroform was then distilled off, and the residual hard cake of crystals broken up and shaken with a large quantity of water, the whole being well cooled during the operation. As soon as all action had subsided, the yellowish-brown precipitate was collected, dried on a porous plate, and dissolved in a large quantity of boiling ethyl alcohol.

The alcoholic solution was concentrated, allowed to stand for 24 hours, and the yellow crystals, which completely filled the liquid, collected, washed with a little alcohol, and dried on a porous plate. The fine, yellow, crystalline mass thus obtained contains two substances which are very readily separated by extraction with boiling benzene, in which the one present in the smallest quantity is very sparingly soluble. The insoluble substance was collected, dried at

100°, and recrystallised from acetic acid; the resulting crystalline mass melted at 236° and showed all the properties of anhydroberberilic acid. The filtrate from the crude anhydroberberilic acid was heated on a water-bath till free from benzene, and the residue recrystallised three times from alcohol.

The beautiful, pale yellow needles thus obtained were free from chlorine; they gave the following results on analysis:—

I. 0·1794 gram substance gave 0·0807 gram H_2O and 0·4064 gram CO_2

0·2813 gram substance gave 8·3 c.c. nitrogen; $t = 19°$; bar. = 740 mm.

II. 0·1696 gram substance gave 0·0775 gram H_2O and 0·3851 gram CO_2.

III. 0·1537 gram substance gave 0·0701 gram H_2O and 0·3483 gram CO_2.

IV. 0·1471 gram substance gave 0·0674 gram H_2O and 0·3335 gram CO_2.

	Theory. $C_{20}H_{19}NO_7$.	Found. I.	II.	III.	IV.	
C.....	62·33	61·78	61·91	61·80	62·24	per cent.
H.....	4·93	4·99	5·07	5·06	5·13	„
N.....	3·63	3·35	—	—	—	„

Each of these analyses was made with a different preparation.

This substance melts at 139—140°, it is readily soluble in hot alcohol, sparingly in the cold; the hot solution, on cooling, deposits the substance in beautiful, slender, pale-yellow needles. It is extremely soluble in benzene and chloroform, very sparingly in light petroleum, and the solutions show a beautiful fluorescence like that exhibited by solutions of quinine. It is insoluble in boiling dilute solutions of alkalis and alkaline carbonates and also in acids, but dissolves readily in warm alcoholic potash. As it seemed probable that this decomposition might throw some light on the constitution of this remarkable substance, about 1 gram was dissolved in dilute alcoholic potash, the solution heated to boiling for a few minutes, diluted with water, and the clear solution nearly neutralised and heated in an open basin on a water-bath until free from alcohol. The liquid was then well cooled, acidified with dilute hydrochloric acid, and the white, semi-solid precipitate which separated, collected, washed with water, and dried on a plate.

The hard mass thus obtained had all the properties of berberilic acid; it was identified by boiling with 50 per cent. sulphuric acid and collecting the crystalline precipitate of anhydroberberilic acid which

formed. This, after recrystallisation from acetic acid, melted at 236°, and gave the following results on analysis :—

0·1510 gram substance gave 0·0630 gram H_2O and 0·3330 gram CO_2.

	Theory. $C_{20}H_{17}NO_8$.	Found.
C.....	60·15 per cent.	60·14 per cent.
H.....	4·26 „	4·63 „

The formation of berberilic acid from a substance of the formula $C_{20}H_{19}NO_7$ by boiling with alcoholic potash is extremely difficult to understand, and although many experiments have been instituted, no clue to the constitution of this remarkable substance has, as yet, been found.

The amount of the substance $C_{20}H_{19}NO_7$ formed in the above decomposition varies very considerably; in some cases as much as 60 per cent. has been obtained, whereas in other experiments, conducted seemingly under exactly similar conditions, anhydroberberilic acid was the principal product.

Amide of Anhydroberberilic Acid,

$$C_{20}H_{16}(NH_2)NO_7 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!N\cdot CH_2\cdot CH_2\cdot CONH_2\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.$$

The substance is readily prepared by the action of ammonia on the chloride of anhydroberberilic acid, thus :—

$$C_{20}H_{16}ClNO_7 + 2NH_3 = C_{20}H_{16}(NH_2)NO_7 + NH_4Cl.$$

The finely-divided chloride was mixed in a sealed tube with a large excess of a strong solution of ammonia in absolute alcohol. On standing in the cold, it was noticed that considerable decomposition took place, and after heating at 100° for five hours, the whole of the chloride had disappeared, and the tube was filled with feathery crystals of the amide. These were collected, washed with alcohol, and dissolved in a considerable quantity of 85 per cent. alcohol; this solution, on cooling, deposited beautiful, colourless, feathery crystals which, after drying at 100°, gave the following numbers on analysis :—

0·1446 gram substance gave 0·0638 gram H_2O and 0·3197 gram CO_2.

0·1888 gram substance gave 11·8 c.c. nitrogen; $t = 20°$; bar. = 746 mm.

	Theory. $C_{20}H_{16}(NH_2)NO_7$.	Found.
C.....	60·30 per cent.	60·36 per cent.
H.....	4·53 „	4·90 „
N.....	7·03 „	7·01 „

This amide melts at 203°. It is readily soluble in boiling alcohol, but only sparingly in the cold; the hot solution, on cooling, deposits the substance as a very voluminous feathery mass, which, when dry, has a fine, satiny lustre.

The amide is insoluble in, and only very slowly hydrolysed by dilute acids; even boiling alcoholic hydrogen chloride seems to have little action on the substance. Alkalis on the other hand, act readily on the amide; on boiling with dilute alcoholic potash, the substance is readily dissolved with evolution of ammonia. The product was mixed with water, nearly neutralised with dilute hydrochloric acid, evaporated until free from alcohol, cooled, and acidified with dilute hydrochloric acid. The white, amorphous precipitate which separated, after being recrystallised from dilute alcohol, showed all the properties of berberilic acid:—

0·1820 gram substance gave 5·2 c.c. nitrogen; $t = 12°$; bar. = 740 mm.

	Theory. $C_{20}H_{19}NO_9$.	Found.
N	3·36 per cent.	3·38 per cent.

The decomposition of this amide into berberilic acid and ammonia by boiling with alcoholic potash takes place according to the equation

$$C_{20}H_{16}(NH_2)NO_7 + 2KOH = C_{20}H_{17}K_2NO_9 + NH_3.$$

Anilide of Anhydroberberilic Acid, $C_{20}H_{16}(NHC_6H_5)NO_7$.

The chloride of anhydroberilic acid reacts readily with aniline in the cold, with evolution of heat and formation of the corresponding anilide:—

$$C_{20}H_{16}ClNO_7 + 2NH_2C_6H_5 = C_{20}H_{19}(NH{\cdot}C_6H_5)NO_7 + C_6H_5NH_2HCl.$$

The finely-powdered chloride was mixed with an excess of pure aniline, allowed to stand for a few minutes, and then gradually heated to 180°. The resulting, almost colourless melt was poured in a thin stream into very dilute hydrochloric acid, the thick, oily precipitate well shaken and stirred until quite solid, collected, washed, and dissolved in boiling 90 per cent. alcohol. On cooling, this solution deposited the anilide in feathery tufts of fine needles. Analysis:—

0·2086 gram substance gave 11·3 c.c. nitrogen; $t = 22°$; bar. = 746 mm.

	Theory. $C_{20}H_{16}(NH{\cdot}C_6H_5)NO_7$.	Found.
N	5·91 per cent.	6·01 per cent.

The anilide melts at 199°. It is readily soluble in hot alcohol and benzene, sparingly in cold alcohol and carbon bisulphide, insoluble in water and light petroleum. It crystallises from alcohol in feathery tufts which, when dry, have a fine, satiny lustre and a distinct, blue fluorescence.

Berberilic Acid,

$$C_{20}H_{19}NO_9 = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CO\cdot NH\cdot CH_2\cdot CH_2\end{matrix}\quad\begin{matrix}COOH\\\end{matrix}>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2.$$

Although almost insoluble in alkalis in the cold, anhydroberberilic acid dissolves readily in dilute aqueous potassium hydrate at a temperature of 30—40° with formation of the potassium salt of berberilic acid:—

$$C_{20}H_{17}NO_8 + 2KOH = C_{20}H_{17}K_2NO_9 + H_2O.$$

In studying this decomposition, very carefully purified anhydroberberilic acid was ground up with water into a fine paste, warmed to about 35°, and potassium hydrate solution then run in, drop by drop, until the whole had dissolved. The clear solution was well cooled, nearly neutralised with hydrochloric acid, cooled again, filtered if necessary, and then an excess of dilute hydrochloric acid added, drop by drop, the liquid being well agitated after each addition. The white, semi-solid precipitate, thus thrown down, was collected, washed with water, and dried on a plate; this preparation consists of practically pure berberilic acid, and as such was employed in all future operations. Considerable difficulty was experienced in obtaining this acid in a crystalline condition; the best results were obtained by dissolving the acid in methyl alcohol, adding about an equal bulk of water, and allowing the solution to stand in an open dish exposed to the air. As the methyl alcohol evaporated, the acid was deposited in the form of a hard, crystalline cake on the bottom of the dish. This was washed with dilute methyl alcohol, dried on a porous plate, and analysed with the following result:—

I. 0·1649 gram substance gave 0·0752 gram H_2O and 0·3449 gram CO_2.

0·3090 gram substance gave 9·0 c.c. nitrogen; $t = 17°$; bar. = 740 mm.

II. 0·1320 gram substance gave 0·0590 gram H_2O and 0·2760 gram CO_2.

	Theory. $C_{20}H_{19}NO_9$.	Found. I.	Found. II.
C	57·55 per cent.	57·01	57·21 per cent.
H	4·55 „	5·06	4·96 „
N	3·36 „	3·30	— „

Berberilic acid melts at about 177—182°, being at the same time decomposed into water and anhydroberberilic acid :—

$$C_{20}H_{19}NO_9 = C_{20}H_{17}NO_8 + H_2O.$$

This melting point is only approximate, as the presence of even traces of impurity causes the substance to soften at a much lower temperature.

It is very readily soluble in methyl and ethyl alcohol. It dissolves appreciably in hot water, and if warm dilute solutions of the salts of the acid are precipitated and filtered, the clear filtrate gradually deposits colourless, granular masses of pure berberilic acid. When heated above its melting point, berberilic acid is completely converted into its anhydride, and the oily product on cooling solidifies to a transparent, fluorescent resin, which will remain in this condition for weeks; in contact with glacial acetic acid, however, this at once becomes crystalline, and after recrystallisation from this solvent, melts at 237°, and consists of pure anhydroberberilic acid.

Basicity of Berberilic Acid.—Two experiments were made with the object of determining the basicity of this acid.

Experiment I.—0·8629 gram of pure anhydroberberilic acid was ground up with water, mixed with 50 c.c. of standard potassium hydrate solution (1 c.c. = 0·005461 gram KOH), warmed to 35°, and kept at this temperature until complete solution had taken place. After the addition of a trace of phenolphthaleïn, 5 c.c. of standard sulphuric acid were required to completely neutralise the product. 0·8629 gram of substance required, therefore, for neutralisation 45 c.c. of potassium hydrate solution = 0·2457 gram KOH; whereas a bibasic acid, $C_{20}H_{19}NO_9$, requires for neutralisation 0·2422 gram KOH.

Experiment II.—0·5355 gram of berberilic acid required 26 c.c. of standard potassium hydrate solution for neutralisation = 0·1419 gram KOH. Theory for a bibasic acid, $C_{20}H_{19}NO_9$ = 0·1438 gram KOH.

Berberilic acid is therefore a *bibasic acid.*

Salts of Berberilic Acid.

Silver salt, $C_{20}H_{17}Ag_2NO_9$. This was prepared as follows:—Pure anhydroberberilic acid was dissolved in a dilute solution of pure potassium hydrate, titrated with dilute nitric acid until only very faintly alkaline, warmed to 30°, and a large excess of silver nitrate added, the whole being violently agitated during the addition. The resulting white precipitate was collected, well washed with water, and dried first on a porous plate over sulphuric acid in a vacuum, and then at 80°.

The analysis gave the following numbers:—

I. 0·2199 gram substance gave 0·0626 gram H_2O, 0·3108 gram CO_2, and 0·0761 gram Ag.

II. 0·2143 gram substance gave 0·0602 gram H_2O, 0·3036 gram CO_2, and 0·0726 gram Ag.

	Theory. $C_{20}H_{17}Ag_2NO_9$.	Found. I.	Found. II.
C	38·08 per cent.	38·52	38·64 per cent.
H	2·70 ,,	3·16	3·12 ,,
Ag	34·32 ,,	34·60	33·88 ,,

This silver salt is very sparingly soluble in water. It is very stable, and only very slowly acted on by light; it may be heated at 100° for a considerable time without undergoing decomposition.

The neutral solution of the potassium salt shows the following behaviour with reagents:—

Zinc Sulphate.—A white, gelatinous precipitate, moderately soluble in hot water, from which it separates on cooling as a white, amorphous mass.

Copper Sulphate.—A light green precipitate, very sparingly soluble in water.

Cadmium Chloride.—A white, amorphous precipitate, soluble in hot water, separating out on cooling very much in the same way as the zinc salt.

Barium Chloride and *Calcium Chloride.*—No precipitate even on boiling.

The *ammonium salt* is mentioned on p. 1038, and its decomposition into ammonia and the ammonium salt of anhydroberberilic acid described.

Dimethyl Salt of Berberilic Acid, $C_{20}H_{17}(CH_3)_2NO_9$ =

$$\begin{matrix} CH_3O \\ CH_3O \end{matrix}\!\!>\!C_6H_2\!<\!\begin{matrix} COOCH_3 \\ CO{-}NH{-}CH_2 \end{matrix} \quad \begin{matrix} COOCH_3 \\ CH_2{-}NH{-}CO \end{matrix}\!\!>\!C_6H_2\!<\!\begin{matrix} O \\ O \end{matrix}\!\!>\!CH_2.$$

This interesting salt is readily prepared by treating silver berberilate with excess of methyl iodide, thus:—

$$C_{20}H_{17}Ag_2NO_9 + 2CH_3I = C_{20}H_{17}(CH_3)_2NO_9 + 2AgI.$$

The pure dry silver salt was ground up, and heated with a large excess of methyl iodide and some pure ether for about two hours in a flask connected with a reflux apparatus. The ether and excess of methyl iodide were then distilled off, and the residue extracted three times with boiling absolute alcohol. The alcoholic solution was

concentrated, and the crop of crystals which separated on standing, collected, washed with a little alcohol, and recrystallised from this solvent. The pure dimethyl salt was thus obtained in the form of long, thin, colourless needles, which, after drying at 100°, gave the following results on analysis:—

0·1590 gram substance gave 0·0756 gram H_2O and 0·3460 gram CO_2.

0·1966 gram substance gave 5·6 c.c. nitrogen; $t = 24°$; bar. = 744 mm.

	Theory. $C_{20}H_{17}(CH_3)_2NO_5$.	Found.
C.....	59·32 per cent.	59·24 per cent.
H.....	5·17 ,,	5·28 ,,
N.....	3·15 ,,	3·15 ,,

Dimethyl berberilate melts at 173—174°. It is readily soluble in hot methyl and ethyl alcohols, but only sparingly in the cold. The hot alcoholic solution, on cooling, deposits the substance in the form of a voluminous mass of snow-white needles, which when dry resemble cotton wool. The dimethyl salt is also readily soluble in hot benzene and xylene, very soluble even in cold chloroform, sparingly in light petroleum and carbon bisulphide. It is readily hydrolysed by boiling with alcoholic potash, with regeneration of berberilic acid.

Action of Heat on Berberilic Acid.

When heated to temperatures not greatly exceeding 180—190°, this acid is converted into anhydroberberilic acid, as already mentioned; but at higher temperatures a much more complicated decomposition sets in, which it is more difficult to follow.

In studying this change, 8 grams of the pure acid was melted in a flask heated in a paraffin-bath, and the temperature gradually raised to 250°, and kept at this for 10 minutes. Abundance of steam and some carbon dioxide were liberated, the substance became darker and darker, and on cooling solidified to a dark brown, almost black resin. This was dissolved in boiling glacial acetic acid, the solution separated from a small quantity of black, insoluble matter by filtration, and the acetic acid evaporated off on a water-bath. The residue was boiled with dilute potassium hydrate solution, which removes nearly all the black resin, leaving a light greenish powder. This was well washed, dried on a porous plate, and extracted with boiling light petroleum (b. p. 90—110°), filtered from insoluble matter, and allowed to stand for 24 hours. The almost colourless

crystals which separated were recrystallised from water, dried at 100°, and analysed with the following result:—

I. 0·1612 gram substance gave 0·0740 gram H_2O and 0·3710 gram CO_2.

0·1715 gram substance gave 10·8 c.c. nitrogen; $t = 14°$; bar. = 746 mm.

II. 0·1495 gram substance gave 0·0679 gram H_2O and 0·3452 gram CO_2.

	Theory. $C_{10}H_9NO_3$.	Found. I.	Found. II.
C	62·82 per cent.	62·76	62·97 per cent.
H	4·71 „	5·10	5·04 „
N	7·33 „	7·40	— „

This substance melts at 181°—182°, and is identical with ω-amidoethylpiperonylcarboxylic anhydride (p. 1013); it was, in fact, the first sample of this substance obtained.

The dark brown alkaline solution which was separated from the crude substance $C_{10}H_9NO_3$, as described above, gave with hydrochloric acid a dark brown, amorphous precipitate. Boiling water dissolved the greater part of this precipitate, leaving a dark, resinous substance, which was separated by filtration. After treatment with animal charcoal, the hot aqueous solution deposited, on cooling, a light yellowish, crystalline powder, which, after repeated recrystallisation, became almost colourless, and gave the following numbers on analysis:—

0·1158 gram substance gave 0·0510 gram H_2O and 0·2430 gram CO_2.

	Theory. $C_8H_8O_4$.	Found.
C	57·14 per cent.	57·23 per cent.
H	4·76 „	4·89 „
O	38·09 „	37·88 „

This acid melts at 245—247°, and when strongly heated in a stream of air, it gives a white, needle-shaped sublimate. It is readily soluble in hot water and alcohol, but sparingly so in the cold. The aqueous solution gives with ferric chloride a slight brownish coloration, and reduces ammoniacal nitrate of silver solution very readily. The acid dissolves in sulphuric acid, and on heating the solution to 100°, an intense green coloration is produced, which on standing becomes reddish-brown.

There can be no doubt that this substance is identical with isovanillic acid (methylprotocatechuic acid),

$$\begin{matrix} HO \\ CH_3O \end{matrix}\!\!>\!C_6H_3\cdot COOH \quad [CH_3O : OH : COOH = 1 : 2 : 4],$$

which Foster and Matthiessen (*Annalen*, Suppl. **2**, 378) obtained by the action of hydrogen chloride on hemipinic acid.

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COOH\end{matrix} + HCl = \begin{matrix}HO\\CH_3O\end{matrix}\!>\!C_6H_3\cdot COOH + CH_3Cl + CO_2.$$

Isovanillic acid melts at 250°, and has properties very similar to those described above.

At the high temperature employed, berberilic acid is evidently first split up into hemipinic acid and the anhydride $C_{10}H_9NO_3$ (see p. 1013); the hemipinic acid is then further decomposed by the steam evolved into isovanillic acid, carbon dioxide, and methyl alcohol, thus:—

$$C_{10}H_{10}O_6 + H_2O = C_8H_8O_4 + CH_3\cdot OH + CO_2.$$

Hydrolysis of Berberilic Acid. Preparation of ω-Amidoethylpiperonylcarboxylic Acid, $C_{10}H_{11}NO_4 = CH_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\CH_2\cdot CH_2\cdot NH_2\end{matrix}$.

Although anhydroberberilic acid is scarcely attacked by boiling dilute acids, berberilic acid is very readily decomposed by this treatment, with formation of hemipinic and amidoethylpiperonylcarboxylic acids, thus:—

$$C_{20}H_{19}NO_9 + H_2O = C_{10}H_{10}O_6 + C_{10}H_{11}NO_4.$$

This decomposition is best carried out as follows:—Anhydroberberilic acid, which should be as pure as possible, is dissolved in dilute potassium hydrate solution at 40°, the solution filtered, acidified, and the precipitated berberilic acid collected, washed, and ground up into a thin paste with water. 10 grams of this acid, in the form of paste, is mixed with 200 c.c. of 5 per cent. sulphuric acid, and the mixture vigorously boiled in a flask connected with a reflux apparatus. Decomposition sets in immediately, and in a short time the greater portion of the acid has passed into solution, giving place to a small quantity of a voluminous precipitate which floats in the liquid. The product is filtered, the precipitate washed well, dried on a porous plate, and recrystallised from acetic acid. The colourless, glistening needles thus obtained melt at 236°, and consist of pure anhydroberberilic acid. Analysis:—

0·1975 gram substance gave 0·0812 gram H_2O and 0·4332 gram CO_2.

	Theory. $C_{20}H_{17}NO_8$.	Found.
C	60·15 per cent.	59·82 per cent.
H	4·26 „	4·56 „

The amount of anhydroberberilic acid formed in this hydrolysis varies with the strength of the sulphuric acid employed. Under the above conditions, 10—15 per cent. of the berberilic acid is converted into anhydroberberilic acid, $C_{20}H_{17}NO_8$, whereas, if 50 per cent. sulphuric acid is used, as much as 50 per cent. of this acid is produced.

The acid solution containing the principal products of the reaction is evaporated to 100 c.c. and extracted at least 20, but better 30, times with small quantities of ether; the ethereal solution, which has a beautiful blue fluorescence, is washed with a little water, dried over calcium chloride, and evaporated, and the solid residue spread on a plate to remove traces of oily mother liquor. The crude hemipinic acid thus obtained may be purified by recrystallisation from water, but it is better to first convert the crude acid into its calcium salt and then to decompose this with hydrochloric acid. For this purpose, the crude acid is dissolved in warm water, neutralised with sodium hydrate, the solution filtered, cooled well, and mixed with a large excess of a strong solution of calcium chloride. The clear solution is then heated to boiling, the heavy, sandy precipitate of the calcium salt which forms, collected, washed with hot water, and dissolved in a small quantity of hot very dilute hydrochloric acid. This solution, on standing, deposits pure hemipinic acid in beautiful, lustrous prisms, which, after drying at 100°, gave the following results on analysis:—

I. 0·1430 gram substance gave 0·0595 gram H_2O and 0·2770 gram CO_2.

II. 0·1375 gram substance gave 0·0561 gram H_2O and 0·2678 gram CO_2.

	Theory. $C_{10}H_{10}O_6$.	Found. I.	Found. II.
C	53·10 per cent.	52·82	53·12 per cent.
H	4·42 „	4·61	4·52 „
O	42·48 „	42·57	42·36 „

Allowing for regenerated anhydroberberilic acid, the amount of hemipinic acid obtained is very nearly theoretical.

During the extraction with ether, a quantity of a white precipitate generally separates, which consists of the sulphate of the new base $C_{10}H_{11}NO_4$; this is best removed by filtration from time to time, otherwise it is difficult to separate the ethereal and aqueous layers effectually. The acid liquors, which should be as free from hemipinic acid as possible, are carefully evaporated to about 50 c.c., care being taken to stop the evaporation as soon as any signs of charring are noticed. This solution, after standing for two days, deposits a large crop of beautifully-formed tabular crystals of the sulphate of the base

$C_{10}H_{11}NO_4$. These are collected, washed with a little water, dissolved in a small quantity of warm water, and barium hydrate solution carefully added until the sulphuric acid is *exactly* precipitated, care being taken that there is no excess of barium hydrate present in the liquid. The filtrate from the barium sulphate is evaporated at a gentle heat (70—80°) on a water-bath until sufficiently concentrated, and allowed to stand 24 hours, when a fine crop of slightly brownish, tabular crystals will have separated. These are collected, washed with a little water, and recrystallised from warm water. The air-dried crystals contain approximately one molecule of water of crystallisation, which is given off gradually over sulphuric acid in a vacuum, but much more readily at 100°, the crystals becoming quite opaque.

0·3141 gram substance, heated at 100° till constant, lost 0·0234 gram.

0·4384 gram substance, heated at 100° till constant, lost 0·0328 gram.

	Theory.	Found.	
	$C_{10}H_{11}NO_4 + H_2O$.	I.	II.
H_2O	7·93 per cent.	7·45	7·49 per cent.

The crystals, dried at 100°, gave the following results on analysis :—

I. 0·1598 gram substance gave 0·0802 gram H_2O and 0·3372 gram CO_2.

0·1087 gram substance gave 6·2 c.c. N; $t = 15°$; bar. = 738 mm.

II. 0·1060 gram substance gave 0·0542 gram H_2O and 0·2228 gram CO_2.

	Theory.	Found.	
	$C_{10}H_{11}NO_4$.	I.	II.
C	57·42 per cent.	57·54	57·32 per cent.
H	5·26 „	5·57	5·68 „
N	6·70 „	6·70	— „

This beautiful substance melts at 180—182° with evolution of gas. It is sparingly soluble in alcohol, benzene, acetone, and carbon bisulphide, readily soluble in hot water, moderately soluble in cold water.

On slowly cooling a moderately concentrated aqueous solution of the base, beautiful, tabular crystals gradually form. Professor Haushofer was kind enough to examine these for me, and has sent the following description :—

"The crystals of the base $C_{10}H_{11}NO_4$ belong to the *monoclinic* system, and represent the simple combination, 0P : ∞P. Owing to the predominance of the basal surface, the crystals have a tabular form. The following angles were measured :—

"∞P : ∞P (clinodiagonal prism face)	78° 53′
0P : ∞P (angle of the base and prism face).	101° 22′."

Salts of the Base $C_{10}H_{11}NO_4$.

This substance has very feeble acid properties, but, on the other hand, its basic properties are well marked, and it combines with acids, forming well-characterised salts.

The *sulphate*, $(C_{10}H_{11}NO_4)_2,H_2SO_4 + 2H_2O$, crystallises from water in beautiful, colourless prisms, readily soluble in hot, moderately so in cold, water. It melts at about 202—203° with decomposition. The water of crystallisation was determined in a sample of the salt which had stood for some days exposed to the air.

I. 0·9246 gram substance, heated at 100° till constant, lost 0·0592 gram.

II. 0·8680 gram substance, heated at 100° till constant, lost 0·0537 gram.

	Theory. $(C_{10}H_{11}NO_4)_2,H_2SO_4 + 2H_2O$.	Found. I.	Found. II.
H_2O	6·40 per cent.	6·29	6·19 per cent.

For analysis, the substance was dried at 100° until the weight was constant.

0·2050 gram substance dissolved in water and acidified with hydrochloric acid gave, on precipitation with barium chloride, 0·0942 gram $BaSO_4$.

0·1470 gram substance gave 0·0612 gram H_2O and 0·2514 gram CO_2.

	Theory. $(C_{10}H_{11}NO_4)_2,H_2SO_4$.	Found.
C	46·51 per cent.	46·64 per cent.
H	4·65 „	4·60 „
SO_4.....	18·60 „	18·93 „

The *hydrochloride*, $C_{10}H_{11}NO_4,HCl$, crystallises from water in colourless, microscopic needles, readily soluble in water, very sparingly in solutions containing much free hydrochloric acid.

The salt, dried over sulphuric acid, does not lose weight at 100°, and, therefore, contains no water of crystallisation. The following results were obtained on analysis:—

0·1376 gram substance gave 0·0621 gram H_2O, and 0·2450 gram CO_2.

0·5292 gram substance, dissolved in water, acidified with nitric acid, and precipitated with nitrate of silver, gave 0·3076 gram AgCl.

	Theory. $C_{10}H_{11}NO_4,HCl$.	Found.
C	48·90 per cent.	48·56 per cent.
H	4·89 „	5·02 „
Cl.....	14·42 „	14·39 „

The Acid Oxalate, $C_{10}H_{11}NO_4,C_2H_2O_4$.—This beautiful salt is readily obtained by mixing a warm concentrated solution of the base with a considerable excess of oxalic acid and allowing the mixture to cool slowly. After standing for some time, long, pale-yellow needles make their appearance, and continue to grow until they almost fill the liquid. The crystals were collected, allowed to remain on a porous plate at the ordinary temperature for some days, and then analysed:—

0·1616 gram substance gave 0·2860 gram CO_2 and 0·0650 gram H_2O.

	Theory. $C_{10}H_{11}NO_4,C_2H_2O_4$.	Found.
C	48·16 per cent.	48·26 per cent.
H.....	4·35 „	4·47 „

It is readily soluble in hot water, moderately in cold water. It melts at about 202—203° with decomposition and rapid evolution of gas.

The Platinochloride, $(C_{10}H_{11}NO_4)_2,H_2PtCl_6$.—This was prepared by adding platinum chloride to the hot strong solution of the hydrochloride of the base, and allowing the solution to stand over night. The beautiful mass of light-reddish needles was collected, washed with water, recrystallised from this solvent, dried at 100°, and analysed.

I. 0·1940 gram substance gave 0·0557 gram H_2O, 0·2046 gram CO_2, and 0·0459 gram Pt.
II. 0·4568 gram substance gave 0·1074 gram platinum.
III. 0·3578 „ „ 0·0832 „
IV. 0·2291 „ „ 0·0542 „

	Theory. $(C_{10}H_{11}NO_4)_2,H_2PtCl_6$.	Found. I.	II.	III.	IV.	
C	29·00 p. c.	28·77	—	—	—	p. c.
H. ...	2·90 „	3·19	—	—	—	„
Pt	23·50 „	23·66	23·51	23·25	23·66	„

This salt crystallises from water in long, slender, straw-coloured needles, which, when rapidly heated in a capillary tube, became dark-coloured at about 200°, and melt with rapid decomposition at 222° with evolution of gas; when slowly heated, it becomes dark at 195—200°, and decomposes completely at about 212°.

The Aurochloride, $C_{10}H_{11}NO_4,HAuCl_4$.—This double salt is precipitated on the addition of gold chloride to a strong solution of the hydrochloride of the base as a light, chocolate-coloured, crystalline

mass. It was dissolved in a little boiling water, filtered from a small quantity of a red, insoluble substance, and the solution allowed to stand for some hours. The crystalline precipitate which separated was collected, washed, dried at 100°, and analysed with the following result:—

0·3354 gram substance gave 0·1204 gram of gold.

	Theory. $C_{10}H_{11}NO_4,HAuCl_4$.	Found.
Au.....	35·87 per cent.	35·89 per cent.

This salt thus obtained forms a chocolate-coloured, crystalline powder, which can be recrystallised from water, but not without slight decomposition.

Action of Heat on the Base $C_{10}H_{11}NO_4$.

In recrystallising this substance from boiling water, it was repeatedly noticed that if the boiling is continued for some time, decomposition takes place, and, instead of the thick, tabular plates of the original substance, thin, glittering plates were deposited as the solution cooled. These were collected, recrystallised from water, and analysed with the following results:—

0·1794 gram substance gave 0·0821 gram H_2O and 0·4125 gram CO_2.

0·1623 gram substance gave 10·1 c.c. N; $t = 16°$; bar. = 740 mm.

	Theory. $C_{10}H_9NO_3$.	Found.
C.....	62·82 per cent.	62·71 per cent.
H.....	4·71 „	5·08 „
N.....	7·33 „	7·30 „

This substance is identical with the anhydride $C_{10}H_9NO_3$ previously described (p. 1013).

The base $C_{10}H_{11}NO_4$ is also decomposed when heated for some little time at its melting point, and the residue, after recrystallisation from water, consists of the pure anhydride $C_{10}H_9NO_3$; it is therefore probable that the temperature 181—182°, given as the melting point of the base $C_{10}H_{11}NO_4$, is, more correctly, the temperature at which this substance is converted into the anhydride $C_{10}H_9NO_3$.

The explanation of this decomposition is that the compound $C_{10}H_{11}NO_4$, being both an acid and a base, on heating is converted into its inner anhydride, thus:—

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2\cdot NH_2\end{matrix} = CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot NH\\CH_2\cdot CH_2\end{matrix} + H_2O.$$

Action of Methyl Iodide on the Substance $C_{10}H_{11}NO_4$.

In assigning the correct constitution to this base, it was very important to obtain a methyl derivative which on heating would yield oxyhydrastinine, thus:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2\cdot NH\cdot CH_3} =$$

$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot N\cdot CH_3}_{CH_2\cdot CH_2}> + H_2O.$$

With this object, the following experiments were instituted:—

1. The finely-divided base was dried at 100° and heated with a large excess of methyl iodide on a water-bath for two hours.
2. The pure, dry base was dissolved in methyl alcohol and heated in a sealed tube at 100° with excess of methyl iodide for one hour.
3. The base (1 mol.) was dissolved in methyl alcohol, a solution of potassium hydrate (1 mol.) in methyl alcohol added, and the whole heated with excess of methyl iodide at 100° for two hours.
4. Sodium ethylate was substituted for potassium hydrate in Experiment 3.

In no case could any methylated base be isolated, but in nearly every experiment an almost quantitative yield of the anhydride $C_{10}H_9NO_3$ was obtained. It is possible that the methylation of the base might take place at lower temperatures, but as the synthesis of oxyhydrastinine was accomplished in another way (p. 1034), these experiments were not continued.

Dibenzoylamidoethylpiperonylcarboxylic Acid,

$$C_{24}H_{19}NO_6 = CH_2<^{O}_{O}>C_6H_2<^{COO\cdot CO\cdot C_6H_5}_{CH_2\cdot CH_2\cdot NH(CO\cdot C_6H_5)}\ (?).$$

As all attempts to prove the presence of an amido-group in the substance $C_{10}H_{11}NO_4$ by means of methyl iodide had failed, experiments were next tried on the action of benzoyl chloride on the base, and good results were obtained by using this reagent, together with sodium hydrate solution (Baumann's method). 2 grams of the pure base was dissolved in warm water, and 50 c.c. of 10 per cent. sodium hydrate solution and 7 grams of benzoyl chloride added alternately in small quantities at a time, the whole being well cooled during the operation. The reddish, resinous substance which separated was collected, washed with water, dissolved in boiling methyl

alcohol, and the solution, after being concentrated considerably, allowed to stand 24 hours. At the end of this time, a quantity of almost colourless crystals had separated; these were collected, washed well with methyl alcohol, recrystallised from this solvent, and analysed with the following result:—

0·1492 gram substance gave 0·064 gram H_2O and 0·3781 gram CO_2.

0·1446 gram substance gave 4·3 c.c. nitrogen; $t = 14°$; bar. = 747 mm.

	Theory. $C_{24}H_{19}NO_6$.	Found.
C.....	69·09 per cent.	69·10 per cent.
H.....	4·56 „	4·79 „
N.....	3·35 „	3·42 „

This beautiful substance melts at 148—150°, with slight previous softening. It is moderately soluble in hot alcohol, chloroform, and benzene, but only sparingly in these liquids in the cold, and almost insoluble in water and light petroleum. It is insoluble in aqueous hydrochloric acid and in ammonia in the cold, and seems to be only very slowly attacked by these reagents on boiling. This behaviour would seem to indicate that hydrogen atoms, both in the amido- and carboxyl-groups in the substance $C_{10}H_{11}NO_4$, had been replaced by benzoyl as shown in the formula assigned to this substance at the head of this section.

Action of Nitrous Acid on Amidoethylpiperonylcarboxylic Acid. Formation of Hydroxyethylpiperonylcarboxylic Acid (p. 1020).

In order to further confirm the formula assigned to the base $C_{10}H_{11}NO_4$, its behaviour towards nitrous acid was carefully studied.

2 grams of the pure base was dissolved in 100 c.c. of warm water, 1 gram of pure sodium nitrite added, and then dilute hydrochloric acid (2 c.c. concentrated HCl and 10 c.c. water) gradually poured in, pieces of powdered ice being thrown in from time to time to prevent the temperature from rising. As the clear solution, even on standing, gave no precipitate, it was heated to boiling on a sand bath for five minutes, and evaporated to about 50 c.c. Abundance of nitrogen and some nitrous acid were evolved during the decomposition, and on standing a crystalline precipitate separated, which was collected, washed with water, recrystallised from this solvent, and analysed with the following results:—

I. 0·1448 gram substance gave 0·0577 gram H_2O and 0·3310 gram CO_2.

II. 0·1619 gram substance gave 0·0638 gram H_2O and 0·3698 gram CO_2.

	Theory. $C_{10}H_8O_4$.	Found. I.	Found. II.
C.....	62·50 per cent.	62·34	62·79 per cent.
H.....	4·16 „	4·43	4·37 „
O.....	33·33 „	32·23	32·84 „

This substance melts at 126°, and is identical with *hydroxyethylpiperonylcarboxylic anhydride*, obtained by the action of potassium hydrate on the nitroso-compound, $C_{10}H_8N(NO)O_3$ (p. 1020). Its formation in the present instance is readily understood from the following equations:—

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2\cdot NH_2} + NOOH =$$

$$CH_2<^{O}_{O}>C_6H_2<^{COOH}_{CH_2\cdot CH_2\cdot OH} + H_2O + N_2 =$$

$$CH_2<^{O}_{O}>C_6H_2<^{CO\cdot O}_{CH_2\cdot CH_2} + 2H_2O + N_2.$$

The yield of the substance $C_{10}H_8O_4$ obtained in this reaction was good, but not quantitative.

Synthesis of Anhydroberberilic Acid.

As this substance is produced from berberilic acid by the action of heat, and as berberilic acid on hydrolysis yields hemipinic acid and the base $C_{10}H_{11}NO_4$, it was thought probable that by combining these two substances under suitable conditions a partial synthesis of anhydroberberilic acid might be accomplished.

With this object, the hemipinic salt of the base $C_{10}H_{11}NO_4$ was first prepared as follows:—1·2 grams of hemipinic acid, dissolved in 10 grams of water, was mixed with 1 gram of the base $C_{10}H_{11}NO_4$ (dissolved in 20 grams of water), the solution evaporated to a small bulk, and allowed to stand in a cold place. After 48 hours, a quantity of peculiar light yellow balls, grouped together in reniform masses, had separated. These were collected, washed with water, dried at 100°, and analysed with the following result:—

0·2798 gram substance gave 7·6 c.c. nitrogen; $t = 19°$; bar. = 750 mm.

	Theory. $C_{20}H_{21}NO_{10}$ ($C_{10}H_{11}NO_4\cdot C_{10}H_{10}O_6$).	Found.
N.....	3·10 per cent.	3·22 per cent.

This salt melts at about 155—160° with decomposition, becoming solid again almost at once. It is readily soluble in hot, moderately in cold water.

The pure, dry salt was now gradually heated to 180° in a wide test-tube in an oil-bath. Decomposition set in at about 160° with frothing and evolution of a quantity of water-vapour; this gradually subsided, and at the end of about 10 minutes the temperature was raised to 200° for a few minutes to complete the reaction. The resulting light brown oil, on cooling, solidified to a hard, transparent resin, which, however, when rubbed with a glass rod moistened with glacial acetic acid, soon became crystalline. The solid mass was ground up and dissolved in boiling 90 per cent. acetic acid, from which it separated on cooling in beautiful, glistening plates. These were collected, recrystallised from acetic acid, and analysed with the following result:—

0·1718 gram substance gave 0·0680 gram H_2O and 0·3786 gram CO_2.

0·2148 gram substance gave 6·3 c.c. nitrogen; $t = 18°$; bar. = 750 mm.

	Theory. $C_{20}H_{17}NO_8$.	Found.
C.....	60·15 per cent.	60·10 per cent.
H.....	4·26 „	4·39 „
N.....	3·51 „	3·41 „

This beautiful substance melts at 236—237°, and is identical in every respect with the anhydroberberilic acid obtained by the oxidation of berberine, as described above (p. 1011). The formation by the above reaction is readily understood from the following equation:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COO\cdot NH_3\cdot CH_2\cdot CH_2\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2 =$$

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!N\cdot CH_2\cdot CH_2\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2 + 2H_2O.$$

The yield of anhydroberberilic acid seemed to be nearly quantitative.

Berberal,

$$C_{20}H_{17}NO_7 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COH\\CO\end{matrix}\!>\!\underset{\displaystyle CO}{\underset{|}{N}}\cdot CH_2\cdot CH_2\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2.$$

The isolation of this substance from the mother liquors of anhydroberberilic acid, $C_{20}H_{17}NO_8$, by dilution with water, as explained in Part I of this research (p. 81), requires very carefully carrying

out, as otherwise the crystals formed are so mixed up with tarry products that their subsequent purification is a matter of the utmost difficulty. In dealing with large quantities of these mother liquors, the bulk of the acetic acid was distilled off, the hot solution mixed with a very small quantity of boiling water, and allowed to stand for at least a week; the sides of the vessel containing it being scratched in several places with a glass rod. If no crystals had then formed, a small quantity more water was added, and the solution again allowed to stand, this treatment being repeated until the crystals deposited are so contaminated with tar that subsequent purification was almost impossible. In any case, a considerable quantity of the substance remains in the mother liquor. The yield varies with different preparations, but is rarely more than 10 grams from 1 kilo. of berberine hydrochloride.

A very pure sample of berberal was subjected to analysis with the following results:—

0·1433 gram substance gave 0·0590 gram H_2O and 0·3289 gram CO_2.

0·1995 gram substance gave 6·5 c.c. N; $t = 18·8°$; bar. = 760 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.	Mean of previous analyses.
C.....	62·66 per cent.	62·53 per cent.	62·66 per cent.
H.....	4·43 „	4·57 „	4·62 „
N.....	3·66 „	3·76 „	3·77 „

The properties of berberal are given in detail in Part I of this research (p. 82).

In the former paper (p. 83), it was mentioned that a solution of 0·7558 gram of berberal in 42·1296 grams of glacial acetic acid (m. p. 16·447°) was employed for the determination of the molecular weight of the substance by Raoult's method. This solution, on standing for 18 months, deposited long, colourless, transparent, prismatic needles; these were collected, washed with a little acetic acid, and drained on a porous plate. The crystals melted, not very sharply, at 115—120°. When heated at 105° for some hours, they became chalky, giving off acetic acid. The residual, very brittle mass melted at 148—150°, and gave, on analysis, the following numbers:—

0·2057 gram substance gave 6·8 c.c. N; $t = 15·5°$; bar. = 740 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.
N.....	3·66 per cent.	3·72 per cent.

The substance was berberal, which, therefore, under certain conditions, crystallises with acetic acid in long, thin, transparent prisms.

Hydrolysis of Berberal. Preparation of Pseudopianic Acid, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COH\\COOH\end{matrix}$ [$CH_3O : CH_3O : COH : COOH = 1 : 2 : 3 : 4$].

The most important property of berberal, and the property which affords the best clue to its constitution, is the decomposition which it undergoes when boiled with dilute sulphuric acid, when it is split up into pseudopianic acid and amidoethylpiperonylcarboxylic anhydride (p. 1013), thus :—

$$C_{20}H_{17}NO_7 + H_2O = C_{10}H_{10}O_5 + C_{10}H_9NO_3.$$

In carrying out this hydrolysis, the very finely-divided pure substance is transferred to a flask connected with a reflux apparatus and boiled briskly with an excess of dilute sulphuric acid (25 per cent.), the whole being vigorously shaken from time to time. In the course of about half an hour, the greater part of the substance dissolves, forming a deep reddish-brown solution, in which a small quantity of a tarry matter swims about. This tarry substance, which completely solidifies on cooling, is collected, washed with water, and recrystallised from alcohol. When analysed, it gave the following result :—

0·1440 gram substance gave 0·0607 gram H_2O and 0·3302 gram CO_2.

	Theory. $C_{20}H_{17}NO_7$.	Found.
C.....	62·66 per cent.	62·53 per cent.
H.....	4·43 „	4·68 „

It melts at 149°, and consists of unchanged berberal.

The conditions in the experiments on the hydrolysis of berberal were very considerably varied, but in every instance similar tarry substances were formed which did not become appreciably less even after six hours' boiling. It is probable that the small quantity of tar always produced coats a certain portion of the berberal, and thus prevents it from coming in contact with the acid; and, indeed, unless the berberal employed be very pure and in a very fine state of division, it is scarcely attacked by boiling dilute sulphuric acid.

The products of the hydrolysis were isolated as follows :—

The acid liquor was evaporated to about three-fourths of its bulk, extracted 20 times with ether, the ethereal solution washed with a little water, and evaporated. The yellowish-white crystalline residue, which contains two substances, was boiled with a little very dilute sodium carbonate solution, until completely dissolved, and the alkaline liquid filtered and allowed to stand in a cold place for some

hours. The crystals which separated were collected, washed with a little water, and recrystallised from this solvent.

They then melted at 182°, and were found to consist of the pure amidoethylpiperonylcarboxylic anhydride $C_{10}H_9NO_3$ (p. 1013).

Analysis :—

0·1153 gram substance gave 0·0536 gram H_2O and 0·2650 gram CO_2.

	Theory. $C_{10}H_9NO_3$.	Found.
C	62·82 per cent.	62·68 per cent.
H	4·71 „	5·16 „

As the anhydride $C_{10}H_9NO_3$ is only sparingly soluble in ether, the amount extracted in this way is small, and the bulk of the substance remains behind in the sulphuric acid liquors. To recover it, the liquors are boiled with excess of barium carbonate, filtered hot, and evaporated to a small bulk; the solution, on cooling, deposits a quantity of crystals of almost pure anhydride, $C_{10}H_9NO_3$.

The alkaline solution from which the small quantity of the anhydride, $C_{10}H_9NO_3$, had crystallised, as described above, was evaporated to half its bulk, cooled well, filtered from a small quantity of the anhydride which separated, and acidified with hydrochloric acid. The beautifully white, crystalline mass which separated was collected, washed with water, and purified by repeated recrystallisation from this solvent. An analysis of a portion of the substance, dried at 100°, gave the following numbers :—

0·1591 gram substance gave 0·0722 gram H_2O and 0·3332 gram CO_2.

	Theory. $CH_3O>C_6H_2<COH$ $CH_3O>\quad\quad<COOH$.	Found.
C	57·14 per cent.	57·13 per cent.
H	4·76 „	5·04 „
O	38·09 „	37·83 „

Pseudopianic acid melts at 121—122°. It is readily soluble in hot water, alcohol, acetone, benzene, and chloroform, sparingly in cold water and light petroleum. It crystallises from hot water in long, slender needles, grouped together to a wool-like mass; from benzene it crystallises in slender needles, and from chloroform in long, flat needles. In its appearance and properties it bears considerable resemblance to opianic acid. When warmed with phenol and much sulphuric acid, a green solution is formed, which, on further heating, becomes violet-brown; the addition of an equal bulk of water to this produces a beautiful violet solution, which, on the careful addition of

alkali, turns first a brilliant blue and finally green. (Compare the Formation of Opiaurin from Opianic Acid. Liebermann and Seidler, *Ber.*, **20**, 873.)

Fusion of Pseudopianic Acid with Potassium Hydrate.—A small quantity of the acid was dissolved in a strong solution of potassium hydrate, the liquid evaporated in a silver dish, and the residue gently fused at about 180—200°. The residue was dissolved in water, acidified with dilute sulphuric acid, and repeatedly extracted with ether. The ethereal solution, on evaporation, deposited a thick, pale-brown syrup, from which, on standing, a small quantity of a crystalline substance separated. The solution of the latter in water gave, with ferric chloride, an intense green coloration, becoming violet, and ultimately red, on the addition of sodium bicarbonate; it also reduced Fehling's solution and ammoniacal nitrate of silver in the cold.

This experiment shows that pseudopianic acid is a catechol derivative.

Estimation of the Methoxyl Groups in Pseudopianic Acid by Zeisel's Method.—The previous experiment showed that pseudopianic acid contains two hydroxyl groups in the ortho-position; but as the acid itself gives no coloration with ferric chloride, it follows that these must be present, either as two methoxy-groups (CH_3O) or as a methylene dioxy-group ($CH_2<^{O}_{O}$). In order to decide this point the action of fuming hydriodic acid on the acid was investigated; the apparatus described by Zeisel (*Monatsh.*, **6**, 995) being employed for the purpose.

0·3726 gram substance was heated with a large amount of fuming hydriodic acid (sp. gr. 1·96), and the escaping methyl iodide, led into an alcoholic solution of silver nitrate, gave 0·8164 gram AgI.

	Theory for $2(OCH_3)$ groups in $C_{10}H_{10}O_5$.	Found.
(OCH_3)...	29·5 per cent.	28·9 per cent.

Pseudopianic acid, therefore, contains two methoxy-groups in the ortho-position.

Basicity of Pseudopianic Acid.—In order to determine the basicity of this acid, a weighed quantity was dissolved in water and titrated with a standard solution of potassium hydrate, with the result that the acid was shown to be *monobasic.*

0·8432 gram substance required for neutralisation 41·3 c.c. of potassium hydrate solution, 1 c.c. of which contained 0·005461 gram KOH.

This corresponds with 0·2256 gram KOH, and agrees closely with the amount required for a monobasic acid, that is, 0·2249 gram.

Salts of Pseudopianic Acid.—In order to prepare the salts of this acid, the pure substance was dissolved in hot water, a slight excess of ammonia added, and the solution allowed to stand over sulphuric acid until quite neutral. On adding silver nitrate to this neutral solution, a white, crystalline precipitate of the *silver salt*, $C_{10}H_9O_5Ag$, was formed. This was collected, well washed with water, dried on a porous plate over sulphuric acid in a vacuum, and analysed with the following result:—

0·1960 gram substance gave 0·0569 gram H_2O, 0·2709 gram CO_2, and 0·0662 gram Ag.

	Theory. $C_{10}H_9O_5Ag$.	Found.
C	37·85 per cent.	37·70 per cent.
H	2·84 ,,	3·22 ,,
Ag	34·07 ,,	33·77 ,,

This salt, when examined under the microscope, is seen to consist of slender needles; these are moderately readily soluble in hot water, and when heated in a capillary tube decompose at about 195° with blackening.

A dilute neutral solution of the ammonium salt shows the following behaviour with reagents:—

Copper Sulphate.—A pale green, amorphous precipitate, especially on warming.

Lead Acetate.—A white, amorphous precipitate, soluble in hot water.

Zinc Sulphate.—A white, amorphous precipitate, more readily produced in warm solutions.

Calcium Chloride and *Barium Chloride.*—No precipitate.

The *potassium salt* of pseudopianic acid separates from its concentrated solution in long, transparent needles, on the addition of strong potassium hydrate solution (sp. gr. 1·4). It is very readily soluble in water.

Action of Potassium Hydrate on Pseudopianic Acid. Formation of Veratric Acid, $(CH_3O)_2C_6H_3{\cdot}COOH$ [$CH_3O : CH_3O : COOH = 1 : 2 : 4$].

According to Matthiessen and Forster (*Annalen*, Suppl. **1**, 332), opianic acid is decomposed by boiling concentrated potassium hydrate into meconine and hemipinic acid, thus:—

$$2\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COH\end{matrix} = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CH_2\end{matrix}\!>\!O + \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COOH\end{matrix}$$

Pseudopianic acid, when similarly treated, is acted on quite differently, the products of its decomposition being veratric and formic (?) acids, thus :—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COH\\COOH\end{matrix} + 2KOH = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_3\cdot COOK + H\cdot COOK + H_2O.$$

In studying this decomposition, the acid was dissolved in a little dilute potassium hydrate, an excess of a concentrated solution of potassium hydrate (sp. gr. 1·4) added, and the whole boiled for one hour. The potassium salt of pseudopianic acid, which first separates out, dissolves readily on warming, and the solution, although it remains quite clear, becomes slightly yellow as the reaction proceeds. The product was diluted with a considerable quantity of water, acidified with hydrochloric acid, and extracted ten times with pure ether. The ethereal solution, after washing with a little water and drying over calcium chloride, deposited, on evaporation, a yellowish, crystalline residue, which, after repeated recrystallisation from hot water, was obtained pure, in the form of colourless needles.

Analysis :—

0·1308 gram substance gave 0·0640 gram H_2O and 0·2855 gram CO_2.

	Theory. $C_9H_{10}O_4$.	Found.
C	59·34 per cent.	59·53 per cent.
H	5·49 „	5·44 „
O	35·17 „	35·03 „

The acid melts at 176—178°. It is readily soluble in hot, but only sparingly in cold water; the hot solution, on cooling, deposits the substance in slender needles. It is also readily soluble in alcohol and ether, and its aqueous solution gives no coloration with ferric chloride. From the results of the analysis and the study of the properties of this substance, there can scarcely be a doubt that it is veratric acid, which melts at 179·5°.

In order, however, to be certain of the identity of the two substances, the acid from pseudopianic acid was converted into the voluminous, crystalline silver salt, and this, after careful drying, digested for half an hour with methyl iodide and a quantity of pure ether. The ethereal solution was filtered from the precipitated silver iodide, evaporated, and the residual, colourless, crystalline mass purified by repeated recrystallisation from a mixture of benzene and light petroleum. In this way, the methyl salt was obtained in the form of colourless needles melting at 58—59°; this corresponds

exactly with the melting point of methyl veratrate. Unfortunately the amount of methyl salt obtained was too small for analysis; but a direct comparison of the acid and its methyl salt with veratric acid and its methyl salt left no doubt as to the identity of the two preparations.

According to the equation at the head of this chapter, which is supposed to represent the action of potassium hydrate on pseudopianic acid, formic acid should be produced. In order to test this, the acid liquors from which the veratric acid had been extracted by ether, as explained above, were distilled in steam. The distillate had a distinctly acid reaction and slight reducing powers, but the quantity of formic acid, which in any case could have been present, was so small, that this test can scarcely be looked on as satisfactory.

Oxime of Pseudopianic Acid, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH{:}NOH\\COOH\end{matrix}$.

In order to prepare this interesting substance, 1 gram of the pure acid was dissolved in dilute potassium hydrate solution (containing 3 grams of KOH), a solution of 1 gram of hydroxylamine hydrochloride in a little water added, and the whole allowed to stand for 24 hours. The product was rendered slightly acid with hydrochloric acid, the white, sandy precipitate which separated collected, washed well, and dried on a porous plate over sulphuric acid in a vacuum. It gave the following results on analysis:—

0·1842 gram substance gave 0·0880 gram H_2O and 0·3577 gram CO_2.

0·1997 gram substance gave 11·2 c.c. N; $t = 20°$; bar. = 740 mm.

	Theory. $C_{10}H_{11}NO_5$,	Found.
C	53·33 per cent.	52·91 per cent.
H	4·88 ,,	5·30 ,,
N	6·22 ,,	6·20 ,,

Pseudopianic oxime melts approximately at 124°, but its melting point could not be accurately determined, owing to the fact that the substance decomposes entirely at about 120° with evolution of gas, and it then becomes quite solid, but melts again at about 215°. The study of this decomposition is given in the next section. Pseudopianic oxime crystallises from water in little balls of needles. It is readily soluble in alkalis and alkaline carbonates, also in hot water and alcohol, but only sparingly so in benzene, chloroform, and light petroleum.

Action of Heat on the Oxime of Pseudopianic Acid.

Formation of Hemipinimide, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>NH.$

The anhydride of the oxime of opianic acid, when heated slightly above its melting point (115°), undergoes a very remarkable molecular change, and is converted into hemipinimide (Liebermann, *Ber.*, **19**, 2924).

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\cdot O\\CH:N\end{matrix} = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>NH.$$

As already stated, the oxime of pseudopianic acid is decomposed at its melting point, and on studying this reaction it was found that in this case also hemipinimide is formed, thus:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH:NOH\\COOH\end{matrix} = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>NH + H_2O.$$

This very important fact proves conclusively that pseudopianic acid has the constitution

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COH\\COOH\end{matrix} \quad [CH_3O : CH_3O : COH : COOH = 1:2:3:4].$$

The conversion of the oxime of pseudopianic acid into hemipinimide may be accomplished in a variety of ways, as, for instance, by boiling with dilute hydrochloric acid; but the simplest method is to heat the substance for about 10 minutes in a test-tube at 160—180°. The crystals first melt, then water vapour is given off, and the whole finally solidifies to a hard, crystalline cake. This is ground up, dissolved in the least quantity of boiling alcohol (it is but very sparingly soluble in this solvent), filtered, and the solution allowed to stand. In a short time needle-shaped crystals separate, which consist of pure hemipinimide.

Analysis:—

0·1856 gram substance gave 11·2 c.c. of nitrogen; $t = 23$; bar. = 755.

	Theory. $C_{10}H_9NO_4$.	Found.
N.....	6·77 per cent.	6·78 per cent.

The substance melted at 224—226°, and showed all the properties of hemipinimide.

Oxime of Opianic Acid, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH:NOH\end{matrix}$.

Liebermann (*Berichte*, **19**, 2923) found that when opianic acid or its ethyl salt is treated in alcoholic solution with hydroxylamine

hydrochloride in the cold, a substance, $C_{10}H_9NO_4$ (opianoxime anhydride), is formed, which would seem to be the inner anhydride of the oxime of opianic acid, $C_{10}H_{11}NO_5$, and he thus seems to draw the conclusion from his experiments that the oxime itself is not capable of existence. This substance may, however, be readily prepared in the following way:—The pure acid (1 mol.) is dissolved in a dilute solution of potassium hydrate (4 mols.), mixed with hydroxylamine hydrochloride ($1\frac{1}{2}$ mols.), and left for 12 hours. If the clear solution is then acidified and allowed to stand, long, slender, needle-shaped crystals separate; these are collected, well washed with water, and dried for some days on a porous plate at the ordinary temperature and then for a few minutes at 50°. This substance is the oxime of opianic acid, as is apparent from the following analytical results:—

0·1630 gram substance gave 0·0738 gram H_2O and 0·3227 gram CO_2.

0·1504 gram substance gave 8·0 c.c. nitrogen; $t = 14°$; bar. = 740 mm.

	Theory. $C_{10}H_{11}NO_5$.	Found.
C.....	53·33 per cent.	53·37 per cent.
H.....	4·88 ,,	5·03 ,,
N.....	6·22 ,,	6·09 ,,

The oxime of opianic acid melts at about 82—83°, but the melting point varies considerably with the rapidity with which the heating is conducted; on further rapid heating, it remains liquid till about 130°, when it suddenly becomes solid, owing to formation of hemipinimide, thus:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\CH{:}NOH\end{matrix} = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!NH + H_2O.$$

This remarkable isomeric change takes place sometimes at much lower temperatures; thus, if the oxime is heated at 80°, after some time the whole becomes converted into a solid cake of hemipinimide. This change is accompanied by the evolution of a very considerable amount of heat (compare Liebermann, *Ber.*, **19**, 2924), and in one case, when an ethereal solution of about 10 grams of the oxime was evaporated on a water-bath, the temperature rose so rapidly as to crack the flask in several places.

The oxime of opianic acid is extremely soluble in alcohol, readily in ether, hot chloroform, and benzene, but only sparingly in light petroleum and carbon bisulphide. It is very readily soluble in warm water, moderately in cold water; the hot solution, on cooling, deposits the substance in needles.

If, however, the aqueous solution is boiled for a short time, decomposition into water and opianoxime anhydride takes place, and on cooling, this anhydride separates in small, colourless, needle-shaped crystals. These, after recrystallisation, and drying, for some days at the ordinary temperature and then for a few minutes at 40—50°, gave the following results on analysis:—

0·1739 gram substance gave 0·0720 gram H_2O and 0·3667 gram CO_2.

	Theory. $C_{10}H_9O_4$.	Found.
C.....	57·97 per cent.	57·51 per cent.
H.....	4·34 „	4·60 „

This substance showed all the properties ascribed to opianoxime-anhydride by Liebermann (*Ber.*, **19**, 2923). The crystals melted apparently at 112—115°, but the mass solidified again at once, owing to its being converted into hemipinimide. This decomposition of the oxime of opiamic acid into its anhydride is probably represented by the equation

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\CH{:}NOH\end{matrix} = \begin{matrix}CH_3\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO{\cdot}O\\CH{:}N\end{matrix} + H_2O.$$

Reduction of Pseudopianic Acid. Formation of Pseudomeconine,

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CH_2\\CO\end{matrix}\!>\!O.$$

Opianic acid is readily reduced by sodium amalgam with formation of meconine (Matthiessen, Foster, *Chem. Soc. J.*, 1863, 446):—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COOH\\COH\end{matrix} + H_2 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CH_2\end{matrix}\!>\!O + H_2O.$$

Pseudopianic acid under the same treatment yields pseudomeconine, thus:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COH\\COOH\end{matrix} + H_2 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CH_2\\CO\end{matrix}\!>\!O + H_2O.$$

1 gram of the pure acid was dissolved in a dilute solution of sodium carbonate, and then 50 grams of $2\frac{1}{2}$ per cent. sodium amalgam gradually added. After standing for 24 hours, the aqueous layer was poured off the mercury, nearly neutralised, filtered, and acidified with hydrochloric acid. The white, crystalline precipitate which separated was collected, washed with water, and recrystallised from this solvent. The crystals obtained melted between 117° and 122°, and were therefore not quite pure; they were dissolved in hot water, the solution cooled until the substance just commenced to crystallise out, two or

three drops of sodium carbonate solution added, and the whole allowed to stand until quite cold. The resulting colourless needles were collected, washed with water, dried at 100°, and analysed with the following result :—

0·1525 gram substance gave 0·0716 gram H_2O and 0·3450 gram CO_2.

	Theory. $C_{10}H_{10}O_4$.	Found.
C.....	61·85 per cent.	61·69 per cent.
H.....	5·16 ,,	5·22 ,,
O.....	32·99 ,,	33·09 ,,

This substance melts at 123—124°, and is in all its properties identical with pseudomeconine, which Salomon (*Ber.*, **20**, 884) obtained by boiling nitrosohemipinimidine with sodium hydrate :—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH_2\\CO\end{matrix}>N(NO) = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH_2\\CO\end{matrix}>O + N_2.$$

Pseudomeconinic Acid, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH_2\cdot OH\\COOH\end{matrix}$.

In experimenting with meconine and pseudomeconine, it was found that although they are very similar in their general reactions, yet they differ widely in the following respect :—

Meconine dissolves readily in dilute sodium hydrate solution with formation of the sodium salt of meconinic acid :—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CH_2\end{matrix}>O + NaOH = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COONa\\CH_2\cdot OH\end{matrix}.$$

On the addition of acids, the free meconinic acid is at once split up into its anhydride, meconine, and water thus :—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot OH\end{matrix} = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CH_2\end{matrix}>O + H_2O.$$

Pseudomeconine is also readily soluble in alkalis, with formation of a salt of pseudomeconinic acid, and on acidifying, the free acid, which is much more stable than meconinic acid, does not decompose, but gradually separates in a pure condition in the form of long, slender, colourless needles. A quantity of this beautiful acid was prepared, washed with water, dried at the ordinary temperature for some days, and then at 40—50° for some minutes, and analysed with the following results :—

0·1446 gram substance gave 0·0728 gram H_2O and 0·3007 gram CO_2.

	Theory. CH_3O CH_3O $>C_6H_2<$ CH_2OH $COOH$.	Found.
C.....	56·60 per cent.	56·71 per cent.
H.....	5·66 „	5·60 „
O.....	37·73 „	37·69 „

Pseudomeconinic acid is very readily converted into pseudomeconine on heating, and it therefore shows practically the same melting point as the latter, the melting of the substance in this case being, however, accompanied by evolution of bubbles of gas (steam). It is much more soluble in water and in most other solvents than pseudomeconine, and differs from its anhydride in the fact that it dissolves readily in a solution of sodium carbonate in the cold. When boiled with water, pseudomeconinic acid dissolves, and, on cooling, beautiful needle-shaped crystals of pseudomeconine separate. In this respect, and in its general behaviour, this acid shows a great similarity to ω-hydroxyethylpiperonylcarboxylic acid,

$$CH_2<\begin{matrix}O\\O\end{matrix}>C_6H_2<\begin{matrix}COOH\\CH_2\cdot CH_2\cdot OH\end{matrix}$$ (p. 1020).

The wide difference in tendency to form inner anhydrides exhibited by two such closely allied substances as meconinic acid and pseudomeconinic acid is very interesting, and experiments are in progress with a view to obtaining further evidence which may throw light on this point.

Salts of Pseudomeconinic Acid.—Pseudomeconinic acid is a strong monobasic acid, as the following experiments show:—

0·3477 gram of the pure acid was dissolved in an excess of standard KOH solution, and the excess titrated back with standard sulphuric acid, using phenolphthaleïn as an indicator. It was found that this amount of substance required for neutralisation 0·0987 gram KOH, whereas on the assumption that a salt, $C_{10}H_{11}O_5K$, had been formed, 0·0915 gram of KOH is required.

Silver Pseudomeconinate, $C_{10}H_{11}O_5Ag$.—To prepare this salt, the pure acid was dissolved in a slight excess of a dilute solution of ammonia, the excess of ammonia allowed to evaporate over sulphuric acid in a vacuum, and the neutral solution precipitated with nitrate of silver. A white, curdy precipitate was obtained, which rapidly became crystalline. It is readily soluble in hot water, and crystallises on cooling in long, slender needles.

Analysis:—

I. 0·1724 gram substance gave 0·0539 gram H_2O, 0·2370 gram CO_2, and 0·0583 gram Ag.

II. 0·4372 gram substance gave 0·1484 gram Ag.

	Theory. $C_{10}H_{11}O_5Ag$.	Found. I.	II.
C.....	37·66 per cent.	37·49	— per cent.
H.....	3·45 „	3·48	— „
Ag.....	33·77 „	33·89	33·94 „

The neutral solution of the ammonium salt gives no precipitatate with lead acetate, barium chloride, or zinc sulphate; a bright green precipitate is produced on the addition of copper sulphate.

Action of Alkalis on Berberal.

Formation of Pseudopianic Acid, $C_{10}H_{10}O_5$; *Pseudopianate of ω-Amidoethylpiperonylcarboxylic Anhydride,* $C_{20}H_{19}NO_8$; *and of ω-Amidoethylpiperonylcarboxylic Anhydride,* $C_{10}H_9NO_3$.

Berberal is insoluble in aqueous alkalis and in alkaline carbonates, but when treated with alcoholic potash, it is readily decomposed, and on the addition of an acid, the above three substances are obtained, the study of which has afforded a clear insight into the constitution of berberal.

In carrying out this hydrolysis, finely powdered berberal is mixed into a thin paste with a little methyl alcohol, heated just to boiling, and then methyl alcoholic potash added drop by drop until the substance has just dissolved, and a drop of the solution mixed with warm water gives only a very slight precipitate. Water is now added, the solution boiled until free from alcohol, acidified with dilute hydrochloric acid, and allowed to stand in a cool place for an hour. A new substance is thus obtained in colourless needles, which, after recrystallisation from water and drying at 100°, gave the following numbers on analysis:—

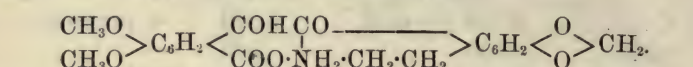
I. 0·1114 gram substance gave 0·0542 gram H_2O and 0·2438 gram CO_2.
0·1180 gram substance gave 3·7 c.c. nitrogen; $t = 18°$; bar. = 725 mm.

II. 0·1540 gram substance gave 0·0714 gram H_2O and 0·3380 gram CO_2.

III. 0·1069 gram substance gave 0·0488 gram H_2O and 0·2336 gram CO_2.

	Theory. $C_{20}H_{19}NO_8$.	Found. I.	II.	III.
C.....	59·85 per cent.	59·58	59·85	59·69 per cent.
H.....	4·74 „	5·20	5·04	5·07 „
N.....	3·49 „	3·58	—	— „

This new substance is the *pseudopianate* of *ω-amidoethylpiperonylcarboxylic anhydride* (p. 1080), and has the constitution



It melts at 149°, and as this temperature corresponds very closely with that noticed as the melting point of berberal (149—150°), it is probable that at this temperature the substance $C_{20}H_{19}NO_8$ is converted into berberal with elimination of water, thus :—

$$C_{20}H_{19}NO_8 = C_{20}H_{17}NO_7 + H_2O,$$

a change which certainly takes place at higher temperatures (p. 1081). The substance $C_{20}H_{19}NO_8$ is readily soluble in boiling water, but only sparingly in cold; the hot solution, on cooling, deposits the substance in the form of slender, colourless needles. It is also readily soluble in methyl and ethyl alcohol and benzene, but only sparingly in light petroleum or carbon bisulphide.

The substance $C_{20}H_{19}NO_8$ is very readily decomposed by alkalis and alkaline carbonates, with formation of pseudopianic acid and *ω*-amidoethylpiperonylcarboxylic anhydride, thus :—

$$C_{20}H_{19}NO_8 + KOH = C_{10}H_9O_5K + C_{10}H_9NO_3 + H_2O.$$

In studying this decomposition, the finely divided substance was mixed with dilute ammonia solution, warmed gently, and shaken vigorously. A considerable portion dissolved, but in a short time a white, crystalline precipitate settled out. This was collected, washed with water, recrystallised from this solvent, and analysed with the following result :—

0·1204 gram substance gave 0·0540 gram H_2O and 0·2778 gram CO_2.

	Theory. $C_{10}H_9NO_3$.	Found.
C.....	62·83 per cent.	62·92 per cent.
H.....	4·71 „	4·98 „

It melts at 181°, and is identical with *ω-amidoethylpiperonylcarboxylic anhydride* (p. 1013).

The filtrate from this substance was boiled on a reflux apparatus for about half an hour, and allowed to stand over night, when an almost colourless, crystalline substance separated, which after recrystallisation from alcohol melted at 149—150°, and showed all the properties of berberal.

The clear alkaline liquid was acidified with hydrochloric acid, and the crystalline precipitate which formed collected, washed with

water, and recrystallised from this solvent. In this way, thin, colourless needles were obtained, which were dried at 100°, and analysed with the following result:—

0·1060 gram substance gave 0·0484 gram H_2O and 0·2219 gram CO_2.

	Theory. $C_{10}H_{10}O_5$.	Found.
C.....	57·14 per cent.	57·09 per cent.
H.....	4·76 „	5·07 „
O.....	38·09 „	37·84 „

This acid melts at 119—120°, and is identical with pseudopianic acid, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COH\\COOH\end{matrix}$, the properties of which are given in detail on p. 1065.

Dilute acids appear to decompose the substance $C_{20}H_{19}NO_8$ with almost as great ease as alkalis. A few crystals of it, boiled in a test-tube with a little 10 per cent. sulphuric acid, rapidly dissolved, and on cooling crystals separated which, after recrystallisation from water, were readily identified as the anhydride $C_{10}H_9NO_3$. Ether extracted from the acid liquor a white, crystalline acid, which showed all the properties of pseudopianic acid. The substance $C_{20}H_{19}NO_8$ is, however, perfectly stable in neutral solutions, and may be recrystallised several times from water without seeming to undergo the least decomposition.

Action of Phenylhydrazine on Berberal.

In order to obtain some further clue to the constitution of berberal, a number of experiments on the behaviour of this substance towards reagents, and especially towards phenylhydrazine, were instituted; but although the conditions of the experiment were varied as much as possible, no definite compound of the two substances could be isolated with certainty.

The following experiment, however, gave interesting results:—2 grams of berberal, 5 grams of phenylhydrazine hydrochloride, 15 grams of crystallised sodium acetate, and about 100 c. c. of 70 per cent. alcohol were heated together in a sealed tube at 130° for four hours. The resulting slightly yellowish solution was transferred to a dish, mixed with water, and gently heated on a water-bath, until all the alcohol had evaporated. During this operation, a reddish-brown, flocculent substance separated, which was collected, washed well with water, and ground up in a mortar with a little methyl alcohol. This treatment removed a sticky, resinous substance, leaving an almost colourless powder, very insoluble in the usual

solvents. It was ultimately purified by repeated recrystallisation from isoamyl alcohol, the crystals well washed, first with isoamyl alcohol, then with methyl alcohol, and dried at 100°.

The analysis gave the following numbers:—

I. 0·1488 gram substance gave 0·0812 gram H_2O and 0·3710 gram CO_2.

0·2052 gram substance gave 25·2 c.c. N; $t = 15°$; bar. = 753 mm.

II. 0·1483 gram substance gave 0·0786 gram H_2O and 0·3684 gram CO_2.

0·2404 gram substance gave 29·5 c.c. N; $t = 17°$; bar. = 756 mm.

III. 0·1654 gram substance gave 0·0950 gram H_2O and 0·4119 gram CO_2.

	Found.			
	I.	II.	III.	
C	68·07	67·75	67·32	per cent.
H	6·06	5·88	6·37	,,
N	14·23	14·40	—	,,

The above analyses, each of which was performed with a different preparation, agree fairly well with either of the two formulæ, $C_{38}H_{37}N_7O_5$ or $C_{22}H_{22}N_4O_3$, thus:—

	$C_{38}H_{37}N_7O_5$.	$C_{22}H_{22}N_4O_3$.
C	67·95 per cent.	67·69 per cent.
H	5·51 ,,	5·65 ,,
N	14·60 ,,	14·36 ,,

The first of these formulæ results from the combination of berberal with three molecules of phenylhydrazine with loss of two molecules of water, thus:—$C_{20}H_{17}NO_7 + 3C_6H_5{\cdot}NH{\cdot}NH_2 = C_{38}H_{37}N_7O_5 + 2H_2O$. The second formula represents the phenylhydrazide of the phenylhydrazine compound of pseudopianic acid, thus:—$C_{10}H_{10}O_5 + 2C_6H_5{\cdot}NH{\cdot}NH_2 = C_{22}H_{22}N_4O_3 + 2H_2O$.

This compound would be represented by the formula

$$\begin{matrix} CH_3O \\ CH_3O \end{matrix}\!\!>\!C_6H_2\!<\!\begin{matrix} CH{:}N_2H{\cdot}C_6H_5 \\ CO{\cdot}NH{\cdot}NH{\cdot}C_6H_5 \end{matrix}.$$

A more careful examination of the course of the reaction appears to favour the latter view. The mother liquors, aqueous as well as alcoholic, from the crude phenylhydrazine compound were mixed with a little dilute hydrochloric acid, evaporated to a small bulk, and filtered hot. The solution on standing deposited a small quantity of brownish plates, which after recrystallisation melted at

178—180°, and showed all the properties of the anhydride $C_{10}H_9NO_3$. It is, therefore, probable that in the above reaction berberal is first decomposed under the influence of water at 180° into the anhydride $C_{10}H_9NO_3$ and pseudopianic acid, and the latter then combines with two molecules of phenylhydrazine as described above. Experiments on the action of phenylhydrazine on pseudopianic acid would settle this point, but these, owing to lack of material, have not yet been instituted.

The phenylhydrazine compound $C_{22}H_{22}N_4O_3$ is very sparingly soluble in water, ethyl and methyl alcohols, benzene, chloroform, and cold amyl alcohol, but readily in hot amyl alcohol; from the latter it crystallises on cooling in small, glistening, yellow needles, which do not melt when heated to 250°. It dissolves readily in hot glacial acetic acid, but does not crystallise out again on cooling. When heated with alcoholic hydrogen chloride, the compound is readily decomposed, with formation of phenylhydrazine hydrochloride.

Synthesis of Berberal.

It has been shown in the preceding sections that berberal is readily decomposed by boiling dilute sulphuric acid into the anhydride $C_{10}H_9NO_3$ and pseudopianic acid; and it appeared extremely interesting to determine whether by bringing these two substances together under suitable conditions berberal might be reproduced, thus:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COH\\COOH\end{matrix} + \begin{matrix}CO\\\|\\NH\cdot CH_2\cdot CH_2\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2 =$$

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}COH\\CO\end{matrix}\!\begin{matrix}CO\\|\\N\cdot CH_2\cdot CH_2\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2 + H_2O.$$

After numerous fruitless experiments, this synthesis was ultimately accomplished by simply heating the two substances together:—0·4 gram of $C_{10}H_9NO_3$ and 0·5 gram of pseudopianic acid were very finely powdered, intimately mixed, and heated in a test-tube gradually to 180°, kept at that temperature for 15 minutes, and then heated at 210° for 15 minutes. During the operation a quantity of water was given off, and the strongly fluorescent, brownish, oily residue solidified to a transparent resin, which cracked all over. This was ground up, dissolved in boiling alcohol, and the solution concentrated and allowed to stand for 24 hours. The sandy, crystalline precipitate which separated was collected, washed with a little alcohol, and twice recrystallised from that solvent. In this way, beautiful glistening plates, were obtained, which melted at 148—150°, and gave the following results on analysis:—

0·1558 gram substance gave 0·0652 gram H_2O and 0·3566 gram CO_2.

0·2310 gram substance gave 7·9 c.c. nitrogen; $t = 22°$; bar. = 745 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.
C	62·66 per cent.	62·42 per cent.
H	4·43 „	4·65 „
N	3·66 „	3·73 „

A careful comparative examination showed that this substance was identical with berberal in every respect, and as the yield obtained was over 60 per cent. of the theoretical, if pseudopianic acid could be obtained in any quantity, the above would be by far the best method for preparing berberal, especially as the resulting product is so very readily purified.

Experiments on the synthesis of pseudopianic acid and of the substance $C_{10}H_9NO_3$ are in progress; as also on the synthesis of berberine from berberal.

Pseudopianate of ω-Amidoethylpiperonylcarboxylic Anhydride,

$$\begin{matrix} CH_3O \\ CH_3O \end{matrix}\!\!>\!C_6H_2\!<\!\begin{matrix} COH \\ COO{-}NH_2{\cdot}CH_2{\cdot}CH_2 \end{matrix}\!\!>\!C_6H_2\!<\!\begin{matrix} O \\ O \end{matrix}\!\!>\!CH_2.$$

In order to prepare this interesting substance, 1·6 grams of ω-amidoethylpiperonylcarboxylic anhydride and 1·8 grams of pseudopianic acid were intimately mixed and dissolved in a little boiling water. The hot solution, on standing, deposited slender needles, which were collected, washed with a little water, recrystallised from this solvent, and analysed with the following result:—

0·1304 gram substance gave 0·0601 gram H_2O and 0·2858 gram CO_2.

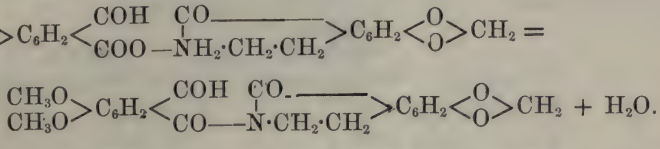
0·1770 gram substance gave 5·5 c.c. nitrogen; $t = 17°$; bar. = 740 mm.

	Theory. $C_{20}H_{19}NO_8$.	Found.
C	59·85 per cent.	59·77 per cent.
H	4·74 „	5·12 „
N	3·49 „	3·55 „

This substance melts at 149°, and is identical with the compound $C_{20}H_{19}NO_8$, obtained by treating berberal with alkalis as explained on p. 1075, and the formation of this substance under these conditions is evidently due to the fact that berberal on hydrolysis first yields pseudopianic acid and ω-amidoethylpiperonylcarboxylic anhydride,

which on solution in water again combine, forming the compound $C_{20}H_{19}NO_8$.

When heated at 180°, the compound $C_{20}H_{19}NO_8$ loses 1 mol. H_2O and is converted into berberal. This interesting decomposition is easily understood with the aid of the equation

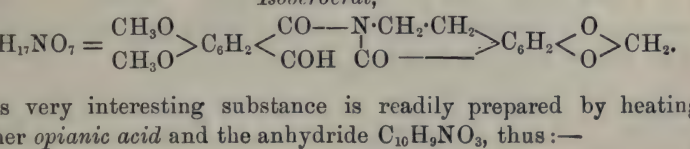


A sample of berberal obtained in this way gave the following results on analysis:—

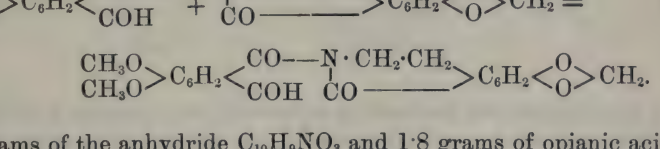
0·0998 gram substance gave 3·2 c.c. nitrogen; $t = 17°$; bar. = 740 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.
N	3·66 per cent.	3·81 per cent.

Isoberberal,



This very interesting substance is readily prepared by heating together *opianic acid* and the anhydride $C_{10}H_9NO_3$, thus:—



1·6 grams of the anhydride $C_{10}H_9NO_3$ and 1·8 grams of opianic acid (prepared from narcotine by oxidation with dilute nitric acid) were ground up together and the mixture heated in a small flask, at 210—215° for thirty minutes. The reaction took place exactly as described in the synthesis of berberal (p. 1079), and the resulting brown, fluorescent oil solidified on cooling to an exactly similar, transparent resin. This was ground up and boiled with a considerable quantity of alcohol until completely dissolved, the solution concentrated, filtered, and allowed to stand for about two hours. The crystalline precipitate, which was slightly greyish and possessed a remarkable satiny lustre, was collected, washed with a little alcohol, dried on a porous plate, and recrystallised from boiling toluene. The solvent leaves undissolved a small quantity of a brownish substance, and on

cooling beautiful, faintly yellow, lustrous plates are obtained, which, after drying at 100°, gave the following results on analysis :—

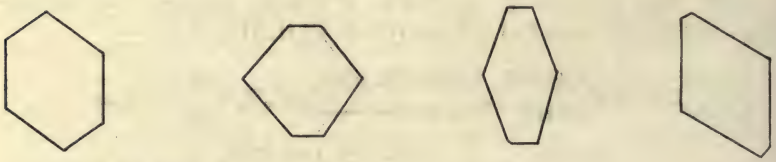
0·1490 gram substance gave 0·0629 gram H_2O and 0·3422 gram CO_2.

0·1986 gram substance gave 6·3 c.c. nitrogen; $t = 15°$; bar. = 740 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.
C	62·66 per cent.	62·53 per cent.
H	4·43 ,,	4·57 ,,
N	3·66 ,,	3·76 ,,

Isoberberal melts at 185° (berberal melts at 149—150°). It is very readily soluble in hot and cold glacial acetic acid, moderately in boiling xylene, toluene, or benzene, and alcohol, but only very sparingly soluble in these solvents in the cold, as also in light petroleum. The solutions fluoresce in exactly the same way as those of berberal.

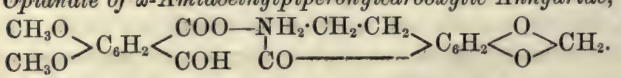
Isoberberal crystallises from boiling xylene in stellate groups, from boiling toluene in flat plates. The best shaped crystals were obtained by allowing a moderately concentrated solution of the substance in hot dilute acetic acid to cool very slowly. Beautiful, colourless crystals were deposited which, when examined under the microscope, were seen to have the following forms :—



Isoberberal, like berberal, is apparently very readily hydrolysed by acids and alkalis, the products being obviously opianic acid and ω-amidoethylpiperonylcarboxylic anhydride.

The yield of isoberberal obtained by the above synthesis is good, and although only small quantities of material have so far been employed, as much as 80 per cent. of pure isoberberal has in one or two cases been obtained.

Opianate of ω-Amidoethylpiperonylcarboxylic Anhydride,



This was prepared by mixing equimolecular parts of opianic acid and ω-amidoethylpiperonylcarboxylic anhydride and dissolving the

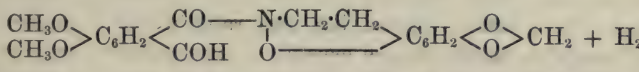
mixture in boiling water. The hot solution, on cooling, deposited the salt in the form of beautiful, feathery groups of needles, which were recrystallised from water and analysed with the following results:—

0·1544 gram substance gave 0·0688 gram H_2O and 0·3394 gram CO_2.

0·2258 gram substance gave 7·1 c.c. nitrogen; $t = 17°$; bar. = 742 mm.

	Theory. $C_{20}H_{19}NO_8$.	Found.
C	59·85 per cent.	59·95 per cent.
H	4·74 „	4·94 „
N	3·49 „	3·56 „

This substance melts at about 130—132° with decomposition. It is readily soluble in hot water, moderately in cold water, extremely soluble in alcohol, but only sparingly in bisulphide of carbon, chloroform, benzene, and light petroleum. It is isomeric with the corresponding pseudopianic salt (p. 1080), and behaves in a manner exactly similar to this salt on heating at 180°, yielding isoberberal:—



The salt was heated at 180° for about ten minutes, and the resulting oil, which solidified to a transparent resin on cooling, recrystallised from boiling toluene. The beautiful, satiny crystals which separated melted at 185° and showed all the properties of isoberberal.

Analysis:—

0·1323 gram substance gave 4·2 c.c. nitrogen; $t = 14°$; bar. = 738 mm.

	Theory. $C_{20}H_{17}NO_7$.	Found.
N	3·66 per cent.	3·74 per cent.

Separation of Oxyberberine, Dioxyberberine, and Anhydroberberilic Acid.

These three compounds occur, together with inorganic salts, in the precipitate which separates from the sulphurous acid liquors on evaporation (p. 1012).

Before proceeding to the separation of the organic compounds, the precipitate is gently warmed with 5 per cent. hydrochloric acid, until the evolution of sulphurous anhydride ceases, filtered, washed

with water, and dried on a porous plate. It is then tested by heating on a platinum spatula, and the treatment with dilute hydrochloric acid repeated if more than traces of inorganic matter are left. The separation of the organic compounds is a matter of some difficulty, but may be accomplished fairly completely by either of the following methods:—

Method I.—The precipitate is boiled with glacial acetic acid, until about two-thirds of it has dissolved; the solution is filtered hot, and the yellow residue, which contains dioxyberberine, washed with a little acetic acid and purified as described on p. 1088. The dark-coloured filtrate is evaporated to half its bulk and allowed to stand in a cool place; in a short time the separation of beautiful, orange-coloured crystals of oxyberberine acetate commences, and at the end of seven days these are collected, washed with acetic acid, dried at 100°, and further purified as described on p. 1085. The dark-coloured mother liquors from these crystals, after evaporation to a small bulk, deposit a further quantity of orange-coloured crystals of oxyberberine acetate, mixed with a small quantity of silky needles of anhydroberberilic acid. These two substances may be separated with difficulty by repeated recrystallisation from glacial acetic acid, but the quantity of either ultimately obtained is but small.

Method II.—The precipitate is dissolved in boiling dilute alcoholic potash, the solution filtered hot and rapidly cooled under the tap. The beautiful, needle-shaped crystals of oxyberberine which separate are collected, washed with alcohol, and purified as described on p. 1085. The alcoholic mother liquor from these is evaporated to about half its bulk, cooled, filtered from a further quantity of oxyberberine which separates, acidified with dilute sulphuric acid, and boiled for a few minutes to decompose any berberilic acid present. The tarry mass which separates is collected, washed with water and repeatedly triturated with hot alcohol; this treatment removes a dark-brown, resinous substance, leaving a yellow, amorphous powder which consists for the most part of dioxyberberine (p. 1087).

Method I is best employed if dioxyberberine is the principal product required, whereas method II appears to give the best yield of oxyberberine.

The relative quantities of these substances present in the crude precipitate varies with almost every preparation, but in one or two cases approximately the following amounts have been obtained from 1 kilo. of berberine hydrochloride:—

Crude yellow precipitate	25 grams.
Oxyberberine	10 „
Dioxyberberine	4 „
Anhydroberberilic acid	2 „

Oxyberberine,

$$C_{20}H_{17}NO_5 = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CH{=}C\text{———}\\CO\text{—}N\cdot CH_2\cdot CH_2\end{matrix}>C_6H_2<\begin{matrix}O\\O\end{matrix}>CH_2\ (?)$$

This interesting substance differs from berberine in containing 1 oxygen atom more than the alkaloïd; it may, therefore, be looked on as the primary product of the oxidation of berberine. It is best purified by recrystallisation either from xylene or from glacial acetic acid. The pure substance dried at 100° gave, on analysis, the following numbers:—

I. 0·1628 gram substance gave 0·0752 gram H_2O and 0·4088 gram CO_2.
0·2457 gram substance gave 8·9 c.c. nitrogen; $t = 25°$; bar. = 740 mm.

II. 0·1635 gram substance gave 0·0743 gram H_2O and 0·4088 gram CO_2.

III. 0·1654 gram substance gave 0·0770 gram H_2O and 0·4162 gram CO_2.

	Theory. $C_{20}H_{17}NO_5$.	Found. I.	II.	III.	
C	68·39 per cent.	68·48	68·19	68·63	per cent.
H	4·84 „	5·13	5·04	5·17	„
N	3·96 „	3·93	—	—	„

This beautiful, yellow substance melts at 198—200° to a deep-yellow liquid, which may be heated to 250° without decomposition; even at 280° it is only slightly discoloured. It is moderately soluble in boiling toluene and xylene, very soluble in hot acetic acid (see below), and still more so in acetic anhydride; sparingly soluble in alcohol and benzene, almost insoluble in light petroleum and water; the alcoholic solution shows a slight blue fluorescence. It crystallises from xylene in beautiful, lustrous, yellow plates. Oxyberberine is slightly soluble in hydrochloric acid, readily so in an alcoholic solution of hydrogen chloride; the addition of alcoholic platinum chloride to this produces a yellow precipitate which appears to be amorphous, but crystallises from alcohol in slender, silky needles.

Oxyberberine is very sparingly soluble in dilute sulphuric acid (1 : 4) but dissolves readily in warm 50 per cent. sulphuric acid, and the yellow solution, on cooling, deposits beautiful, light-yellow needles. It gives the following very delicate reaction, by means of which the smallest trace of the substance may be detected. A minute particle of the substance is dissolved in a little warm 50 per cent. sulphuric acid, cooled, and one drop of ordinary concentrated nitric acid added.

A deep-brown coloration is at once produced, which rapidly changes to an intense violet; on the addition of water the colour is not destroyed, but turns a fine reddish-violet, which is very similar in appearance to the colour of a very dilute solution of permanganate.

Oxyberberine dissolves in a warm solution of hydrogen iodide, and if a trace of iodine is added, a brown precipitate is produced, which crystallises from alcoholic hydrogen iodide in green plates or groups of slender microscopic needles.

In order to determine whether oxyberberine is capable of forming an acetyl derivative, a small quantity of the substance was boiled with an excess of acetic anhydride in a reflux apparatus for four hours, evaporated to a small bulk, and allowed to stand over night. The beautiful, yellow, needle-shaped crystals which formed were collected, washed with acetic anhydride, and dried at 130°.

The analysis showed that the substance was unchanged :—

0·1548 gram substance gave 0·0712 gram H_2O and 0·3904 gram CO_2.

	Theory. $C_{20}H_{17}NO_5$.	Found.
C.....	68·39 per cent.	68·78 per cent.
H.....	4·84 „	5·11 „

Oxyberberine Acetate, $C_{20}H_{17}NO_5,C_2H_4O_2$.

Although oxyberberine, as compared with berberine, is a very feeble base, it forms a very well characterised acetate; this is readily obtained in a pure state by dissolving the substance in boiling glacial acetic acid, and allowing the solution to stand for some days. The acetate gradually separates in beautiful, lustrous, yellow crystals; these are collected, drained on a porous plate, and dried by exposure to the air for three days. An analysis gave the following numbers :—

0·1370 gram substance gave 0·0642 gram H_2O and 0·3238 gram CO_2.

	Theory. $C_{20}H_{17}NO_5,C_2H_4O_2$.	Found.
C.....	64·23 per cent.	64·39 per cent.
H.....	5·11 „	5·21 „

It is moderately stable at ordinary temperatures, if the crystals are large, but the finely-powdered substance gradually loses acetic acid on exposure to the air. A sample of the preparation analysed above was finely powdered and allowed to stand exposed to the air for four days; on analysis it gave C = 65·30 : H = 5·28, and on drying at 100° it lost only 10·9 per cent. of acetic acid.

Dried at 100°, the beautifully lustrous crystals become opaque, and

rapidly lose the whole of their acetic acid, leaving a residue of pure oxyberberine. A small quantity of the acetate dried at 100° for two hours gave, on analysis, the following results:—

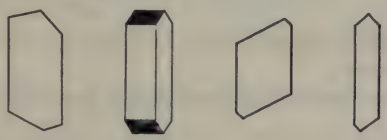
0·1474 gram substance gave 0·0660 gram H_2O and 0·3704 gram CO_2.

	Theory. $C_{20}H_{17}NO_5$.	Found.
C.....	68·39 per cent.	68·53 per cent.
H.....	4·84 „	4·97 „

1·8586 gram of the pure acetate, heated at 100° until the weight was constant, lost 0·2702 gram of acetic acid = 14·54 per cent.

$C_{20}H_{17}NO_5(C_2H_4O_2)$ contains 14·59 per cent. of acetic acid.

The beautiful crystals of oxyberberine acetate, when examined under the microscope, seem to have the following forms:—



As this acetate is moderately easily soluble in glacial acetic acid, its molecular weight was carefully determined by Raoult's method, with the following result:—

Substance taken	1·5730 grams.
Acetic acid taken	100·4 „
Melting point of acetic acid.....	16·262°
„ „ mixture	16·112°
Depression of the melting point...	0·150°
Molecular weight of the substance found from the above data	407
Theory for $C_{20}H_{17}NO_5,C_2H_4O_2$	411

The yield of oxyberberine is about 10 grams from 1 kilo. of berberine hydrochloride, and as it can thus be obtained in considerable quantity, I hope to make it the subject of a future investigation.

Dioxyberberine,

$$C_{20}H_{17}NO_6 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\cdot CH\text{———}\\CO\cdot N\cdot CH_2\cdot CH_2\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}O\\O\end{matrix}\!>\!CH_2\ (?).$$

This remarkable substance, which probably results from the further action of oxidising agents on oxyberberine, is unfortunately produced in such small quantity and is so difficult to purify, that it has

been found impossible to investigate it as thoroughly as could have been wished.

The crude yellow product obtained as explained on p. 1012, is almost insoluble in the usual solvents, but it may be obtained pure by recrystallisation either from boiling aniline, nitrobenzene, or ethyl benzoate, the former being preferable on account of its somewhat lower boiling point. In recrystallising it, the powder is added to boiling aniline as long as it is dissolved, the solution rapidly filtered, and allowed to cool; the whole operation being conducted as quickly as possible, as boiling with aniline decomposes the substance and great loss occurs. The hot solution, on cooling, deposits the new substance in glistening, yellow needles, which are collected, washed first with aniline and then with methyl alcohol, and dried on a porous plate.

For the analysis the substance was dried at 100° for one hour :—

I. 0·1740 gram substance gave 0·0802 gram H_2O and 0·4196 gram CO_2.

0·3469 gram substance gave 11·7 c.c. nitrogen; $t = 16°$; bar. = 766 mm.

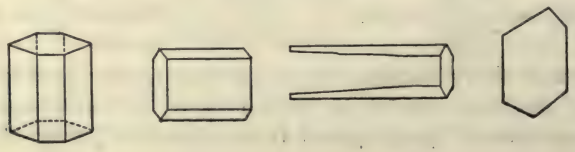
II. 0·1867 gram substance gave 0·0882 gram H_2O and 0·4470 gram CO_2.

III. 0·2272 gram substance gave 0·1013 gram H_2O and 0·5470 gram CO_2.

	Theory. $C_{20}H_{17}NO_6$.	Found. I.	II.	III.	
C....	65·39 per cent.	65·76	65·29	65·66	per cent.
H....	4·64 „	5·17	5·25	4·95	„
N....	3·82 „	3·92	—	—	„

Each of these analyses was made with a separate preparation: I was recrystallised once from aniline; II, twice from the same solvent; and III was recrystallised from ethyl benzoate.

Dioxyberberine is almost insoluble in alcohol, benzene, and light petroleum, sparingly soluble in boiling glacial acetic acid, readily in boiling aniline, nitrobenzene, or ethyl benzoate, but only sparingly in these liquids in the cold. It crystallises from ethyl benzoate in small, well-defined crystals, which, when examined under the microscope, are seen to have the following forms :—



Some of the crystals were very curiously striated: twin crystals were frequent, as also single examples with very imperfectly formed edges.

Dioxyberberine shows the following characteristic reactions:—

It dissolves in concentrated sulphuric acid, producing a reddish-violet solution; on warming, the colour gradually changes and ultimately becomes intensely olive-green.

It dissolves in nitric acid with a fine violet colour. If a drop of nitric acid is added to its solution in cold concentrated sulphuric acid, a beautiful, deep bluish-violet coloration is produced, which is destroyed on the addition of water (compare the corresponding reaction with oxyberberine, p. 1085).

Finely-divided dioxyberberine is turned a dark green by the addition of a few drops of concentrated hydrochloric acid; on warming with an excess of hydrochloric acid, the greater part dissolves, forming a yellowish-green solution, which, on addition of a drop of platinum chloride, gradually becomes intensely violet-coloured.

Action of Alkalis on Dioxyberberine.

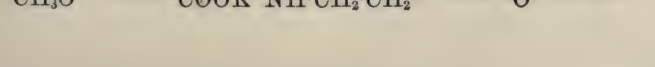
Although only sparingly soluble in aqueous solutions of alkalis, dioxyberberine dissolves with great readiness in warm alcoholic potash, forming a deep orange-red solution, which, if sufficiently concentrated, deposits on cooling, beautiful, deep orange-coloured needles of a potassium salt. In order, if possible, to obtain this in a state pure enough for analysis, pure dioxyberberine was dissolved in a strong solution of pure potassium hydrate in 80 per cent. methyl alcohol, the solution allowed to stand, and the crystals which separated quickly collected, washed with a little methyl alcohol, spread on a porous plate, and transferred to a vacuum desiccator.

Two separate preparations gave the following results on analysis:—

1. 0·2179 gram substance gave, after decomposition with sulphuric acid, 0·0404 gram K_2SO_4 = 8·31 per cent. of K.
2. 0·3371 gram substance gave 0·0698 gram K_2SO_4 = 8·09 per cent. K.

Theory for $C_{20}H_{18}NO_7K$	9·22	per cent. K.
„ „ $C_{20}H_{18}NO_7K + 3H_2O$ ..	8·17	„ K.

Unfortunately, owing to the small amount of material at my disposal, it was not possible to make any further analyses of this interesting salt, but it seems probable that when dioxyberberine dissolves in alcoholic potash it forms a potassium salt of the formula



which crystallises from 80 per cent. methyl alcohol with 3 mols. of water of crystallisation. This potassium salt is partially decomposed by much water, with separation of a small quantity of a yellowish-white substance. Acids decompose the salt with separation of a light ochre-coloured precipitate, which consists of pure dioxyberberine. In order to be certain of this, the precipitate was collected, washed with water and methyl alcohol, dried on a porous plate at 100°, and analysed with the following results:—

0·1595 gram substance gave 0·0685 gram H_2O and 0·3830 gram CO_2.

	Theory. $C_{20}H_{17}NO_6$.	Found.
C.....	65·39 per cent.	65·48 per cent.
H.....	4·63 „	4·77 „

Hydroxylamine has no action on a dilute solution of the potassium salt. In order to prove this, 0·75 gram of pure dioxyberberine was dissolved in a considerable excess of dilute methyl alcoholic potash, 1 gram of hydroxylamine hydrochloride, dissolved in a little water, added, and the solution, after standing for 24 hours, heated to boiling for half-an-hour. The bulk of the methyl alcohol was distilled off, the residue acidified with hydrochloric acid, and the precipitate which separated washed well, and analysed with the following result:—

0·2163 gram substance gave 6·8 c.c. nitrogen; $t = 21°$; bar. = 746 mm.

	Theory. $C_{20}H_{17}NO_6$.	Found.
N.....	3·82 per cent.	3·70 per cent.

The substance was therefore unchanged dioxyberberine.

The most remarkable property of the potassium salt of dioxyberberine is that, on standing in the air, it gradually loses its colour, and is converted into the potassium salt of berberilic acid. In studying this decomposition, 2 grams of pure dioxyberberine was converted into the potassium salt by dissolving it in methyl alcoholic potash, and the product, which consisted of red crystals suspended in a yellow solution, was agitated with air in a large flask for about a week, the whole being gently warmed from time to time. The solution gradually became colourless, and the red crystals ultimately entirely disappeared, giving place to a small quantity of a white, crystalline precipitate. The product was dissolved in water, neutralised with dilute hydrochloric acid, evaporated until free from alcohol, and acidified. The white, semi-solid precipitate of berberilic acid which separated was collected, washed with water, and converted into anhydroberberilic acid by boiling with 50 per cent. sulphuric acid

for a few minutes. The white, crystalline precipitate thus obtained was recrystallised from much alcohol, dried at 100°, and analysed with the following result:—

0·1392 gram substance gave 0·0564 gram H_2O and 0·3070 gram CO_2.

0·1560 gram substance gave 4·8 c.c. nitrogen; $t = 21°$; bar. = 756 mm.

	Theory. $C_{20}H_{17}NO_8$.	Found.
C	60·15 per cent.	60·15 per cent.
H	4·26 „	4·48 „
N	3·51 „	3·49 „

This substance melts at 237° and is identical with anhydroberberilic acid.

The formation of berberilic acid from the potassium salt of dioxyberberine may be explained by the following equation:—

$$C_{20}H_{18}NO_7K + KOH + O_2 = C_{20}H_{17}NO_9K_2 + H_2O,$$

but it is extremely difficult to understand the *modus operandi* of the reaction. In order, however, to prove that oxygen was actually taken up in this reaction, 0·22 gram of dioxyberberine was dissolved in methyl alcoholic potash and placed in a eudiometer in an atmosphere of oxygen over mercury. After remaining for five days, with constant agitation and gentle application of heat from time to time, it was found that 11 c.c. of oxygen had been absorbed. A blank experiment was then carried out with methyl alcoholic potash solution alone, under exactly similar conditions, and, although slight absorption did take place, the diminution in the volume of oxygen after six days was only 3·2 c.c.

This experiment seems to prove that the transformation of dioxyberberine into berberilic acid in alkaline solution is due to the absorption of oxygen from the air.

Further experiments which are in progress will, it is hoped, throw light on this extremely interesting decomposition.

Berilic Acid,

$$C_{20}H_{15}NO_8 = \begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!\!>\!N\cdot CH{:}CH\!>\!C_6H_2\!<\!\begin{matrix}COOH\\O\end{matrix}\!\!>\!CH_2\ (?).$$

The crude residue, obtained as explained on p. 1012 was collected from several operations; it weighed about 6 grams, and formed a semi-solid, dark-greyish mass, from which it was extremely difficult to obtain anything crystalline. It was digested with glacial acetic acid, the dark-green solution filtered, evaporated to a small

bulk, and allowed to stand for about seven days in a cool place. At the end of that time a quantity of glistening plates had separated; these were collected, well washed with glacial acetic acid, and twice recrystallised from this solvent. In this way beautiful, colourless, glistening plates were obtained, which, after drying at 105°, gave the following results on analysis :—

I. 0·1437 gram substance gave 0·0555 gram H_2O and 0·3312 gram CO_2.
0·1725 gram substance gave 5·6 c.c. nitrogen; $t = 15°$; bar. = 730 mm.

II. 0·1638 gram substance gave 0·0618 gram H_2O and 0·3762 gram CO_2.

III. 0·1580 gram substance gave 0·0608 gram H_2O and 0·3633 gram CO_2.

	Theory. $C_{20}H_{15}NO_8$.	Found. I.	II.	III.
C.....	62·99 per cent.	62·85	62·64	62·71 per cent.
H.....	3·94 „	4·29	4·19	4·27 „
N.....	3·67 „	3·71	—	— „

This new acid has therefore probably the composition $C_{20}H_{15}NO_8$. When heated in a capillary tube, it darkens in colour at about 195°, and melts at 198—200° with blackening and evolution of gas; in this respect, the substance differs very markedly from any of the other compounds obtained in this research. It is only sparingly soluble in water, but readily in boiling glacial acetic acid, from which it is deposited on cooling in magnificent, lustrous plates; these, when examined under the microscope, are seen to have the following forms :—

This acid dissolves readily in sulphuric and hydrochloric acids; the solution in hydrochloric acid gives with platinum chloride a yellowish-white, amorphous precipitate, which dissolves moderately easily in hot water, and crystallises out again, on cooling, in yellow needles.

Salts of Berilic Acid.

This acid dissolves readily in alkalis, and gives very characteristic salts. The *ammonium salt* was prepared by dissolving the acid in

excess of ammonia, and allowing the solution to stand over sulphuric acid in a vacuum for some days.

The silver salt, $C_{20}H_{14}AgNO_8$, was obtained, by precipitating the ammonium salt with silver nitrate, as a white, curdy precipitate, somewhat soluble in water. The well-washed salt was dried at 100°, and analysed with the following result:—

0·1966 gram substance gave 0·0570 gram H_2O and 0·3446 gram CO_2.

0·1906 gram substance gave 0·0407 gram Ag.

	Theory. $C_{20}H_{14}AgNO_8$.	Found.
C	47·61 per cent.	47·81 per cent.
H.....	2·78 „	3·22 „
Ag.....	21·43 „	21·35 „

A solution of the ammonium salt shows the following behaviour with reagents:—

Calcium Chloride.—In dilute solutions, at first there is no change, but, on standing, the calcium salt separates in glistening, leafy crystals readily soluble in hot water, sparingly in cold water.

Barium Chloride.—No precipitate in moderately dilute solutions.

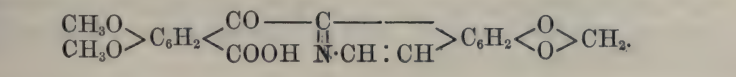
Zinc Sulphate.—Gives at once a white precipitate, consisting of tufts of needles, sparingly soluble in hot water, from which it crystallises on cooling in groups of needles and four-sided plates.

Copper Sulphate.—A light-green, amorphous precipitate, which, on warming, changes to a very light-blue, apparently crystalline precipitate, almost insoluble both in hot and cold water.

Cadmium Chloride.—A white precipitate consisting of minute tufts of needles; it dissolves in much hot water, but is more insoluble than the zinc salt.

Lead Acetate.—A white, curdy precipitate, soluble in hot water, from which it crystallises on cooling in plates, which have almost the same form as the crystals of the acid itself.

A further study of the properties of this interesting acid will, it is hoped, give more definite evidence as to its constitution, which, in the meantime, may either be represented by the formula at the head of this section or by



Hemipinic Anhydride, $\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>O$.

This substance, which is only produced in very small quantities in the oxidation of berberine under the conditions stated on p. 1012, was purified by repeated recrystallisation from glacial acetic acid, and thus obtained in the form of long, slightly brownish needles, which on analysis gave the following numbers:—

I. 0·1554 gram substance gave 0·0548 gram H_2O and 0·3255 gram CO_2.

II. 0·1553 gram substance gave 0·0574 gram H_2O and 0·3266 gram CO_2.

	Theory. $C_{10}H_8O_5$.	Found. I.	Found. II.
C	57·69 per cent.	57·12	57·32 per cent.
H	3·86 „	3·91	4·10 „
O	38·54 „	38·97	38·58 „

This substance melts at 167°, and has properties very similar to those of hemipinic anhydride (m. p. 167°). On studying, however, its behaviour towards alcoholic potash, an acid melting at 146° was obtained instead of hemipinic acid (m. p. 180°), and it was not until the action of alcoholic potash on a sample of hemipinic anhydride prepared from the pure acid itself had been studied that the cause of this reaction could be explained. It was then found that hemipinic anhydride, when boiled with dilute alcoholic potash, is converted into ethyl hydrogen hemipinate:—

$$\begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}CO\\CO\end{matrix}>O + C_2H_5\cdot OH + KOH = \begin{matrix}CH_3O\\CH_3O\end{matrix}>C_6H_2<\begin{matrix}COOC_2H_5\\COOK\end{matrix} + H_2O.$$

0·5 gram of the anhydride from berberine was boiled with dilute alcoholic potash for 10 minutes, mixed with twice its bulk of water, heated on a water-bath until the alcohol was expelled, cooled, and acidified with dilute hydrochloric acid. The white, crystalline precipitate formed was collected, washed with water, and recrystallised from this solvent. In this way, beautifully glistening, colourless needles were obtained, which, on drying at 100°, lost their lustre, and therefore probably contained water of crystallisation. The analysis gave the following numbers:—

I. 0·1456 gram substance gave 0·0748 gram H_2O and 0·3006 gram CO_2.

II. 0·1504 gram substance gave 0·0777 gram H_2O and 0·3115 gram CO_2.

	Theory. $CH_3O>C_6H_2<COOC_2H_5$ $CH_3O \quad\quad COOH$.	Found. I.	Found. II.
C	56·69 per cent.	56·31	56·48 per cent.
H	5·51 „	5·71	5·74 „
O	37·79 „	37·98	37·78 „

It melted sharply at 146°.

According to Anderson (*Annalen*, **86**, 194), ethyl hydrogen hemipinate melts at 132·2°; Wegscheider (*Monats.*, **3**, 369), on the other hand, gives 141—142° as the melting point of this salt.

In order to prove the constitution of this compound, a small quantity was dissolved in dilute sodium hydrate solution, boiled for about 10 minutes, cooled, neutralised with dilute hydrochloric acid, an excess of a strong solution of calcium chloride added, and the whole heated to boiling for a few minutes. The crystalline calcium salt which separated was collected, washed with water, and dissolved in a little hot dilute hydrochloric acid; this solution, on cooling, deposited beautiful, colourless crystals of pure hemipinic acid (m. p. 180°).

The formation of ethyl hydrogen hemipinate by the action of boiling alcoholic potash on hemipinic anhydride is very remarkable, and, in looking over the properties of a series of similar anhydrides, I have not been able to find a parallel case.

Hydrastic Acid, $C_9H_6O_6 = CH_2<^{O}_{O}>C_6H_2<^{COOH}_{COOH}$.

The crude acid solution obtained as described on p. 1013 contains two acids, namely hydrastic acid and hemipinic acid; these were separated and identified as follows:—The aqueous solution was extracted 20 times with ether, the ethereal solution dried over calcium chloride and evaporated, when a pale-yellow syrup was obtained, which, even after standing over sulphuric acid in a vacuum, showed very little sign of crystallising. As all attempts to make this syrup crystallise failed, recourse was had to the following method of purification:—The crude substance was dissolved in water, neutralised with potassium hydrate, the cold solution mixed with a large excess of a strong solution of calcium chloride, filtered, and heated to boiling. This caused the precipitation of a very sparingly soluble calcium salt, which was collected, washed with hot water, and dissolved in a sufficient quantity of boiling 5 per cent. hydrochloric acid. This solution, on cooling, deposited a quantity of brownish, leafy plates which, after repeated recrystallisation and treatment with animal charcoal, were obtained as colourless, glistening plates.

After being dried at 100°, it gave the following numbers on analysis:—

0·1540 gram substance gave 0·0455 gram H_2O and 0·2903 gram CO_2.

0·1520 gram substance gave 0·0434 gram H_2O and 0·2832 gram CO_2.

	Theory. $C_9H_6O_6$.	Found. I.	Found. II.
C	51·43 per cent.	51·41	50·81 per cent.
H	2·86 „	3·27	3·17 „
O	45·71 „	45·32	46·02 „

This acid melts at 180°, is moderately soluble in water, and crystallises from this solvent in colourless, leafy plates.

The silver salt, $C_9H_4Ag_2O_6$, was prepared by dissolving the acid in excess of ammonia, allowing the solution to stand over sulphuric acid in a vacuum until neutral, and then adding an excess of nitrate of silver solution. The white, amorphous precipitate thus produced was collected, washed with water, dried over sulphuric acid in a vacuum, and analysed with the following result:—

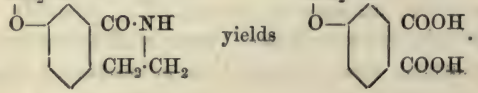
0·2009 gram substance gave 0·0230 gram H_2O and 0·1820 gram CO_2.

0·2966 gram substance gave 0·1506 gram Ag.

	Theory. $C_9H_4O_6Ag_2$.	Found.
C	25·48 per cent.	24·69 per cent.
H	0·94 „	1·27 „
Ag	50·94 „	50·78 „

This acid is therefore bibasic, and is probably identical with hydrastic acid, $C_9H_6O_6$, obtained by Freund and Lachmann (*Ber.*, **22**, 2325), which melts at 175°; as, however, no further description of the properties either of the acid itself or of its salts has as yet been published, it is impossible to speak with certainty of the identity of the two acids.

The presence of hydrastic acid among the products of the oxidation of berberine is readily understood, as this substance would result from the action of oxidising agents on ω-amidoethylpiperonylcarboxylic anhydride or one of its derivatives, thus:—



The first mother liquors from this acid were evaporated, and the syrupy residue heated in a large test-tube at 180—190° for one hour. During this operation water vapour escaped, and a small quantity of a sublimate, consisting of fine, colourless needles, formed in the cooler portions of the tube. The residue was powdered and repeatedly extracted with boiling alcohol, the alcoholic solution concentrated and allowed to stand for some hours; and the crystals which separated, collected, washed with alcohol, and repeatedly recrystallised from this solvent. In this way almost colourless needles were obtained which melted at 167°, and showed all the properties of hemipinic anhydride. It was dissolved in a little boiling alcoholic potash, and the solution diluted with water, and boiled for half an hour. The product was evaporated to a small bulk, acidified with hydrochloric acid, repeatedly extracted with ether, the ethereal solution evaporated, and the residue recrystallised from water. The crystals obtained melted at 178—180°, and showed all the properties of hemipinic acid.

Berberine Hydrogen Sulphite, $C_{20}H_{17}NO_4,H_2SO_3$.

In oxidising berberine with potassium permanganate, a small amount of the alkaloïd always escapes the action of the oxidising agent, and this, during the subsequent treatment with sulphurous acid, is converted into berberine hydrogen sulphite. This very insoluble substance is obtained in small quantity during the purification of anhydroberberilic acid (p. 1014) as a light yellow precipitate; and for a long time its constitution was a matter of doubt, as it seemed very improbable that a sulphite of berberine could be so sparingly soluble in water. It was purified by recrystallisation from very large quantities of water, dried at 100°, and analysed with the following results:—

I. 0·1734 gram substance gave 0·0749 gram H_2O and 0·3629 gram CO_2.

0·2319 gram substance gave 7 c.c. nitrogen; $t = 19°$; bar. = 748 mm.

1·4174 gram substance, boiled with dilute nitric acid until the evolution of nitrous fumes had ceased, largely diluted with water, and precipitated with barium chloride, gave 0·7750 gram $BaSO_4$.

II. 0·1188 gram substance gave 0·0504 gram H_2O and 0·2510 gram CO_2.

	Theory. $C_{20}H_{17}NO_4,H_2SO_3$.	Found. I.	Found. II.
C	57·55 per cent.	57·08	57·62 per cent.
H	4·55 „	4·80	4·71 „
N	3·36 „	3·48	— „
SO_4.....	23·02 „	22·71	— „

This salt is remarkably stable, and crystallises from dilute solutions of potassium carbonate unchanged. It dissolves readily in dilute nitric acid, and on cooling berberine nitrate crystallises out.

0·1712 gram substance gave 0·0740 gram H_2O and 0·3799 gram CO_2.

	Theory. $C_{20}H_{17}NO_4HNO_3$.	Found.
C	60·30 per cent.	60·40 per cent.
H	4·52 „	4·80 „

Berberine hydrogen sulphite dissolves readily in dilute hydrochloric acid, and on the addition of platinum chloride a yellow precipitate of berberine platinochloride is thrown down.

This was collected, washed with water, dried at 100°, and analysed with the following result:—

0·2284 gram substance gave 0·0718 gram H_2O and 0·3708 gram CO_2.

0·3739 gram substance gave 0·0670 gram Pt.

	Theory. $(C_{20}H_{17}NO_4)_2,H_2PtCl_6$.	Found.
C	44·47 per cent.	44·22 per cent.
H	3·33 „	3·49 „
Pt	18·02 „	17·96 „

As soon as the composition of this substance had been determined in this way, confirmatory experiments were made, with the object of preparing this salt directly from berberine; and it was found that when a solution of berberine hydrochloride is mixed with a solution of sodium hydrogen sulphite containing an excess of sulphurous acid, a precipitate is produced which has properties exactly similar to those of the salt described above. It was not thought necessary to analyse it.

Examination of the Mother Liquors of Berberilic Acid and of Berberal.

Using the methods of separation described in the preceding sections, the actual weight of crystalline substances obtained by oxidising 1 kilo. of berberine hydrochloride is only about 350—400

grams; at least half the product remains in the alcoholic mother liquors of berberilic acid and in the acetic acid mother liquors of berberal (pp. 1041, 1063, and Trans., 1889, pp. 78 and 81).

These, on evaporation, deposit thick, almost black, tarry masses, from which only small quantities of crystalline substances could be obtained by treatment with solvents. As, however, it seemed probable that very interesting compounds might be contained in these tars, the investigation of which might throw additional light on the question of the constitution of berberine, a large number of experiments were instituted with the object of decomposing these tars and thus obtaining crystalline decomposition products, the study of which would reveal the nature of the compounds actually contained in the tars. After numerous failures, the following method gave unexpectedly good results:—

The *mother liquors* of *berberilic acid* were first experimented with. These were gently heated in a dish on a water-bath until free from alcohol, and the black residue boiled briskly in a large, enamelled pan with a considerable quantity of 8—10 per cent. sulphuric acid; the whole being well stirred during the operation. After boiling for two hours, the greater portion had dissolved, forming an orange-coloured solution; this was allowed to cool, decanted from the undissolved tar, and the latter again boiled with fresh dilute sulphuric acid, the operation being continued until only a small quantity of a pitch-like substance remained, which was not further acted on by the sulphuric acid.

The resulting liquors were treated by one of the two following methods:—

Method I.—The liquors were extracted 20 times with ether; the resulting, almost colourless, flocculent ethereal solution, on standing in a cold place, deposited a quantity of crystals. These were collected, washed with ether, and recrystallised twice from water, and in this way beautiful, lustrous plates were obtained, which, after drying at 100°, gave the following numbers on analysis:—

0·1510 gram substance gave 0·0638 gram H_2O and 0·3175 gram CO_2.

0·2010 gram substance gave 6·5 c.c. nitrogen; $t = 21°$; bar. = 740 mm.

	Theory. $C_{20}H_{19}NO_9$.	Found.
C.....	57·55 per cent.	57·34 per cent.
H.....	4·55 „	4·69 „
N.....	3·35 „	3·47 „

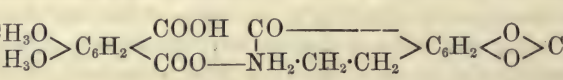
This substance melts at 180°, and is identical with the compound $C_{20}H_{19}NO_9$, described in Part I of this research (p. 84); it is

isomeric with berberilic acid, from which it differs in the following point:—The substance dissolves readily in hot dilute sodium carbonate solution, and, on standing, lustrous crystals of the substance $C_{10}H_9NO_3$ (p. 1013) separate, and the alkaline liquors, on examination, are found to contain hemipinic acid, which can be isolated as its calcium salt in the usual way (p. 1095). A quantitative determination of the relative amounts of these decomposition products formed gave the following results:—

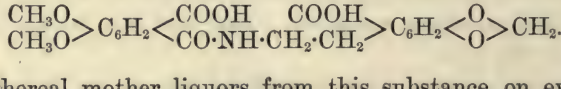
1·18 grams of substance yielded 0·49 gram of the anhydride $C_{10}H_9NO_3$ and 0·66 gram of calcium hemipinate. The compound $C_{20}H_{19}NO_9$ is therefore decomposed according to the equation

$$C_{20}H_{19}NO_9 + Na_2CO_3 = C_{10}H_9NO_3 + C_{10}H_8O_6Na_2 + CO_2.$$

according to which 1·18 grams should have yielded 0·54 gram of the substance $C_{10}H_9NO_3$ and 0·74 gram of calcium hemipinate. The substance is therefore the hydrogen hemipinic salt of $C_{10}H_9NO_3$, and has the following constitution:—



Berberilic acid, with which this substance is isomeric, has the following somewhat similar constitution:—



The ethereal mother liquors from this substance, on evaporation, deposited considerable quantities of a yellow, crystalline mass, which, on examination, was found to be almost pure hemipinic acid. It was purified by means of the calcium salt, recrystallised twice from water, and the beautifully colourless, lustrous prisms thus obtained were analysed with the following results:—

0·1258 gram substance gave 0·0528 gram H_2O and 0·2446 gram CO_2.

	Theory. $C_{10}H_{10}O_6$.	Found.
C	53·09 per cent.	53·02 per cent.
H	4·42 „	4·66 „
O	42·48 „	42·32 „

0·5610 gram substance, dried at 100°, lost 0·0792 gram.

$C_{10}H_{10}O_6 + 2H_2O$ contains 13·74 per cent. of water of crystallisation.

Found..... 14·11 „ „ „ „

The sulphuric acid mother liquors, from which the substance, $C_{20}H_{19}NO_9$ and hemipinic acid had been separated by extraction with

ether, were mixed with just sufficient baryta-water to remove the sulphuric acid, filtered, and the yellow filtrate evaporated to a small bulk. The solution, on standing, deposited crystals, which were found to consist of a mixture of the substances $C_{10}H_{11}NO_4$ (p. 1055) and $C_{10}H_9NO_3$ (p. 1013), and in this way considerable quantities of these substances were prepared for use in subsequent work.

From these experiments, it appears that the tarry substances contained in the alcoholic mother liquors of berberilic acid still contain large quantities of this acid, which is hindered from crystallising by the presence of a small quantity of a black, tarry decomposition product.

Method II.—The acid liquors were evaporated to the crystallising point, without extracting with ether, and set aside to crystallise. After standing for seven days, the almost colourless, crystalline cake which had formed at the bottom of the dish was separated from the mother liquor, washed with a little water, and drained on a porous plate. The liquors were then carefully evaporated, allowed again to crystallise, the operation being continued as long as crystals separated. The various crops of crystals were mixed, boiled with sufficient water to completely dissolve them, the solution filtered, allowed to stand for two days, the crystals which separated collected, and recrystallised twice from water. In this way, magnificent, pale-yellow, lustrous crystals were obtained which on analysis gave the following numbers :—

I. 0·1308 gram substance gave 0·0608 gram H_2O and 0·2746 gram CO_2.

0·1910 gram substance gave 7·3 c.c. nitrogen ; $t = 15°$; bar. = 750 mm.

II. 0·1450 gram substance gave 0·0648 gram H_2O and 0·3096 gram H_2O and 0·3096 gram CO_2.

0·2310 gram substance gave 9·6 c.c. nitrogen ; $t = 12°$; bar. = 740 mm.

III. 0·1512 gram substance gave 0·0765 gram H_2O and 0·3201 gram CO_2.

0·2526 gram substance gave 10·0 c.c. nitrogen ; $t = 20°$; bar. = 742 mm.

IV. 0·1518 gram substance gave 0·0680 gram H_2O and 0·3250 gram CO_2.

0·1338 gram substance gave 5·1 c.c. nitrogen ; $t = 18°$; bar. = 750 mm.

	Theory. $C_{30}H_{30}N_2O_{13}$.	Theory. $C_{30}H_{28}N_2O_{12}$.	Found. I.	II.	III.	IV.
C	57·51 p. c.	59·21 p. c.	57·19	58·22	57·74	58·38 p. c.
H	4·79 „	4·57 „	5·17	4·96	5·62	4·97 „
N	4·47 „	4·57 „	4·40	4·80	4·40	4·32 „

Each of these analyses was made with a different preparation.

The formula $C_{30}H_{30}N_2O_{13}$ represents the *hemipinate* of the substance $C_{10}H_9NO_3$, crystallising with one molecule of water = $(C_{10}H_9NO_3)_2C_{10}H_{10}O_6 + H_2O$; the formula $C_{30}H_{28}N_2O_{12}$ represents the anhydrous salt; it is probable that the former is the correct formula. This beautiful substance melts at about 187—189° if very quickly heated, but if slowly heated it melts at about 177° with decomposition. It is sparingly soluble in alcohol, benzene, and cold water, moderately in hot water, readily soluble in acetic acid.

The pure substance dissolves readily in hot dilute sodium carbonate solution, and on cooling, beautiful plates of the substance $C_{10}H_9NO_3$ separate out, whilst the alkaline solution contains hemipinic acid. When heated at 180—200° for a short time, decomposition sets in, a quantity of water vapour is given off, and the residue dissolved in a little boiling acetic acid deposits, on cooling, crystals of hemipinic anhydride (m. p. 167°). The substance $C_{10}H_9NO_3$ may be obtained from the mother liquors of these crystals by evaporation and recrystallising the residue from water.

The aqueous mother liquors from these yellow crystals contain considerable quantities of a second substance, which is much more readily soluble and crystallises with difficulty. The concentrated liquors on long standing deposit feathery crystals, which are difficult to obtain quite pure, owing to the fact that when recrystallised from water, they are decomposed to some extent with formation of the yellow crystals described above. A very carefully recrystallised sample of this substance gave the following results on analysis:—

0·1602 gram substance gave 0·0772 gram H_2O and 0·2964 gram CO_2.

0·2902 gram substance gave 10·7 c.c. nitrogen; $t = 20°$; bar. = 745 mm.

0·2930 gram substance, dissolved in water, acidified with hydrochloric acid, and precipitated with barium chloride, gave 0·0881 gram $BaSO_4$.

	Theory. $C_{30}H_{34}O_{14}N_2(SO_4)$ = $C_{10}H_{10}O_6(C_{10}H_{11}NO_4)_2,H_2SO_4$.	Found.
C	48·52 per cent.	50·45 per cent.
H	4·59 ,,	5·35 ,,
N	3·77 ,,	4·10 ,,
SO_4	12·94 ,,	12·35 ,,

This substance is a mixed sulphate and hemipinate of the base $C_{10}H_{11}NO_4$. It crystallises from water, in which it is readily soluble, in colourless feathery leaflets, which melt at about 190° with decomposition. The constitution of this salt is readily shown from the following experiment:—

A quantity of the substance was dissolved in warm water, just sufficient barium hydrate solution added to remove all the sulphuric acid, the product filtered, and the clear filtrate evaporated to a small bulk on a water-bath. After standing for two days, peculiar, pale-yellow, nodular crystals had formed; these were collected, washed with water, dried at 100°, and analysed with the following result:—

I. 0·1501 gram substance gave 0·0719 gram H_2O and 0·3053 gram CO_2.

0·2722 gram substance gave 9·5 c.c. nitrogen; $t = 12°$; bar. = 755 mm.

II. 0·2680 gram substance gave 9·9 c.c. nitrogen; $t = 14°$; bar. = 758 mm.

	Theory. $C_{30}H_{32}N_2O_{14}$ = $C_{10}H_{10}O_6(C_{10}H_{11}NO_4)_2$.	Found. I.	Found. II.
C	55·90 per cent.	55·47	— per cent.
H	4·97 ,,	5·32	— ,,
N	4·35 ,,	4·07	4·33 ,,

The formation of this salt from the double salt just described is represented thus—

$$C_{10}H_{10}O_6(C_{10}H_{11}NO_4)_2,H_2SO_4 + Ba(OH)_2 = C_{10}H_{10}O_6(C_{10}H_{11}NO_4)_2 + BaSO_4 + 2H_2O.$$

The di-hemipinate of the base $C_{10}H_{11}NO_4$ is readily soluble in hot and moderately in cold water; it crystallises after long standing in nodular masses somewhat resembling the hydrogen hemipinate of the same base (p. 1061). It melts at about 175° with decomposition; it is moderately soluble in hot alcohol, very readily in acetic acid, and almost insoluble in benzene The strong solution in water, acidified with hydrochloric acid and mixed with platinum

chloride, gives a precipitate of the platinochloride of $C_{10}H_{11}NO_4$, and on extracting the solution with ether, and evaporating the ethereal extract, a residue of hemipinic acid is obtained.

Either of the above methods may be employed for preparing considerable quantities of the substance $C_{10}H_9NO_3$ from the tarry mother liquors of berberilic acid, and both give good results, but, as a rule, method I was adopted in dealing with large quantities of these mother liquors.

Examination of the Mother Liquors of Berberal.

Before experimenting with these mother liquors, the greater bulk of the water and acetic acid was distilled off; the black, tarry residue, which obviously still contained considerable quantities of berberal, was then treated with various solvents with the view of isolating this substance, but without success. The whole of the tar was then boiled with large quantities of 20 per cent. sulphuric acid for some hours, filtered from any undissolved matter, and the reddish-brown solution allowed to stand. In the course of a few days a large quantity of bright-reddish needles had separated, these were collected, washed with water, and recrystallised from very dilute sulphuric acid; a large quantity of bright-yellow needles were obtained which were identified as sulphate of berberine.

The platinochloride prepared from this salt gave on analysis the following numbers :—

0·3271 gram substance gave 0·0587 gram platinum.

	Theory. $(C_{20}H_{17}NO_4)_2,H_2PtCl_4$.	Found.
Pt.....	18·02 per cent.	17·94 per cent.

In one case, in which 1 kilo. of berberine hydrochloride had been oxidised, in the usual way, nearly 100 grams of unchanged berberine sulphate was recovered from the mother liquors of berberal by the above method.

The mother liquors from which the berberine sulphate had crystallised were concentrated, and extracted 20 times with ether; the solution on evaporation deposited a quantity of almost colourless crystals, which could not be obtained pure, but which appeared for the most part to consist of the pseudopianic salt of the substance $C_{10}H_9NO_3$ (m. p. 149°, see p. 1080). The whole quantity was dissolved in boiling sodium carbonate solution; this solution, on cooling, deposited colourless crystals of the anhydride $C_{10}H_9NO_3$, and the

alkaline solution contained a considerable quantity of pseudopianic acid.

The sulphuric acid liquors which had been extracted with ether still contain a large amount of the substance $C_{10}H_9NO_3$, which may be extracted by precipitating the sulphuric acid with baryta-water and evaporating the solution. The product thus obtained is, however, very crude and difficult to purify.

These experiments seem to prove that the mother liquors of berberal and of berberilic acid do not contain any other products than those already described in this paper.

Examination of the Aqueous Mother Liquors from the Oxidation of Berberine (p. 1013).

These aqueous mother liquors, from which the bulk of the neutral organic substances had been extracted by ether, deposited, on evaporation, a quantity of a solid residue, which on examination was found to contain large quantities of organic matter.

As it was important to determine the nature of these organic substances, some qualitative experiments were first instituted. To a portion of the solution, phosphomolybdic acid was added, the precipitate which formed collected, washed, treated with alkalis, and the white, crystalline mass which separated recrystallised from water. In this way colourless plates were obtained, which after recrystallisation from water melted at 181—182°, and consisted of the anhydride $C_{10}H_9NO_3$ (p. 1013).

A second portion of the solution was acidified, extracted several times with ether, the ethereal solution evaporated, the residue neutralised, boiled with calcium chloride, and the precipitate which formed dissolved in a little hot dilute hydrochloric acid. After standing for some time, an acid separated which showed all the properties of hemipinic acid, but which seemed to be mixed with small quantities of another acid. In order to determine approximately the amount of hemipinic and other acids present in the solution, the liquors from 1 kilo. of berberine hydrochloride were neutralised, mixed with a large quantity of a saturated solution of calcium chloride, and heated to boiling for half an hour. The precipitate which formed was collected on cloth bags, well washed with hot water, and extracted with hot dilute hydrochloric acid, until no more organic matter passed into solution. The acid solution was filtered from the mass of calcium sulphate which is necessarily always present, evaporated to the crystallising point, and the dark-brown crystalline crust which separated on cooling dissolved in dilute sodium

carbonate solution and boiled with freshly ignited animal charcoal for one hour. The pale-yellow filtrate was neutralised with hydrochloric acid, boiled with calcium chloride, the calcium salt which separated decomposed with hydrochloric acid, and the acid thus obtained recrystallised from water. The white, crystalline powder which was deposited from the hot solution was dried at 100°, and analysed with the following result:—

I. 0·1450 gram substance gave 0·0552 gram H_2O and 0·2808 gram CO_2.

II. 0·1550 gram substance gave 0·0550 gram H_2O and 0·3016 gram CO_2.

III. 0·1562 gram substance gave 0·0573 gram H_2O and 0·3016 gram CO_2.

	Theory. $C_{10}H_{10}O_6$.	Theory. $C_9H_6O_6$.	Found. I.	II.	III.
C....	53·10 p. c.	51·43 p. c.	52·81	53·06	52·66 p. c.
H...	4·42 „	2·86 „	4·22	3·94	4·07 „
O....	42·48 „	45·71 „	42·97	43·00	43·27 „

These analyses were made with different preparations.

This substance melts at 165—168° with decomposition and evolution of gas. It shows all the properties of hemipinic acid, and undoubtedly consists for the most part of this substance contaminated with a second acid (hydrastic acid?) which contains much less hydrogen.

In order to prove the presence of hemipinic acid, about 2 grams of the substance was heated at 200° for one hour, and the residue recrystallised twice from glacial acetic acid. The beautiful, colourless needles thus obtained melted at 167°, and showed all the properties of hemipinic anhydride.

Analysis:—

0·1552 gram substance gave 0·0554 gram H_2O and 0·3272 gram CO_2.

	Theory. $\begin{matrix}CH_3O\\CH_3O\end{matrix}\!>\!C_6H_2\!<\!\begin{matrix}CO\\CO\end{matrix}\!>\!O$.	Found.
C	57·69 per cent.	57·49 per cent.
H	3·84 „	3·96 „
O	38·46 „	38·55 „

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, March*, 1890. Vol. LVII.]

ETHYL $\alpha\alpha_1$-DIACETYLADIPATE.

By W. H. Perkin, Jun., Ph.D.

Ethyl sodioacetoacetate and ethylene bromide, when heated together, react readily with elimination of sodium bromide and formation of an almost colourless oil, which consists for the most part of two substances, mixed always with varying quantities of unchanged ethylene bromide and ethyl acetoacetate.

The first of these (which has already been described in detail in this Journal, 1885, **47**, 801; 1887, **51**, 820) is ethyl acetyltrimethylenecarboxylate, produced according to the equation—

$$2\,\frac{CH_3\cdot CO}{COOC_2H_5}\!>\!CHNa + BrCH_2\cdot CH_2Br =$$

$$\frac{CH_3\cdot CO}{COOC_2H_5}\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5 + 2NaBr.$$

The second substance, which has been called ethyl $\alpha\alpha_1$-diacetyladipate, is the product of the direct action of 1 mol. of ethylene bromide on 2 mols. of ethyl sodioacetoacetate, thus:—

$$2\,\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CHNa + BrCH_2\cdot CH_2Br =$$
$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 2NaBr.$$

Some time since, I carried out, in conjunction with M. Obrembsky (*Berichte*, **19**, 2045), a short investigation of this substance, in the course of which we obtained several interesting derivatives; these however, we were then able to examine only superficially.

During the progress of some researches on the internal condensation of diketones, on which I am at present engaged, it became necessary to repeat all the experiments originally carried out with ethyl diacetyladipate, and also to institute a number of new ones; and I beg now to lay the results obtained before the Society.

Ethyl diacetyladipate cannot be separated by fractional distillation from the ethyl acetyltrimethylenecarboxylate and other impurities which accompany it, as by this treatment it undergoes a more or less complete decomposition even when distilled under greatly reduced pressure (50 mm.); an almost perfect separation may, however, be accomplished by distilling the crude product obtained in the action of ethylene bromide on ethyl sodioacetoacetate in a current of steam. By this treatment, all the ethyl acetyltrimethylenecarboxylate as well as unchanged ethylene bromide and ethyl acetoacetate pass over along with the water, leaving in the retort a thick, oily residue, which consists of slightly impure ethyl diacetyladipate.

From this, pure ethyl diacetyladipate may be obtained by two methods:—

I. The crude substance, dissolved in ether, is treated with sodium ethylate, and the precipitated disodium-compound collected, washed free from impurities, and decomposed by an acid—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CNa\cdot CH_2\cdot CH_2\cdot NaC\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + H_2SO_4 =$$
Disodium compound.
$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + Na_2SO_4.$$
Ethyl diacetyladipate.

II. The crude product is treated with concentrated alcoholic ammonia, the crystalline diamido-compound which separates collected, purified by recrystallisation, and decomposed by dilute hydrochloric acid—

$$\begin{matrix} CH_3\cdot C\cdot NH_2 & NH_2\cdot C\cdot CH_3 \\ \| & \| \\ COOC_2H_5\cdot C\cdot CH_2 & -\ CH_2\cdot C\cdot COOC_2H_5 \end{matrix} + 2HCl + 2H_2O =$$

Ethyl diamidodiethyladipate.

$$\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix} CO\cdot CH_3 \\ COOC_2H_5 \end{matrix} + 2NH_4Cl.$$

Pure ethyl diacetyladipate is a thick, colourless oil, possessing properties very similar to those noticed in the case of mono-substituted derivatives of ethyl acetoacetate.

When heated with 2 mols. of phenylhydrazine on a water-bath, it yields as primary product, ethyl diphenylhydrazinediacetyladipate,

$$\begin{matrix} CH_3\cdot C(N_2H\cdot C_6H_5) \\ COOC_2H_5 \end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix} C(N_2H\cdot C_6H_5)\cdot CH_3 \\ COOC_2H_5 \end{matrix},$$

a yellowish-white, crystalline substance which melts at 145°, and, when heated, readily loses 2 mols. of alcohol being converted into bis-phenylmethylmethylenepyrazolone,

$$\begin{matrix} C_6H_5\cdot N & & & & N\cdot C_6H_5 \\ & \diagdown\diagup & & & \diagdown\diagup \\ & N \quad CO & & & CO \quad N \\ & \| \quad | & & & | \quad \| \\ CH_3\cdot C & -CH\cdot CH_2\cdot & CH_2\cdot & CH & -C\cdot CH_3. \end{matrix}$$

This pyrazolone-derivative crystallises from acetic acid in white needles, which are almost insoluble in most organic solvents, and do not melt at 250°. In its other properties this interesting substance shows considerable similarity to other pyrazolones substituted in the methylene-group.

The careful study of the products of the distillation of ethyl diacetyladipate has led to very interesting results.

This substance, when fractioned under diminished pressure (225 mm.), distils, with apparently very slight decomposition, as a yellow oil, only a small quantity of a thick, dark-coloured residue remaining in the retort. The oily distillate, on repeated distillation, yields a large fraction boiling constantly at 230—231° (225 mm.), which, on analysis, gives numbers agreeing with the formula $C_{14}H_{20}O_5$.

Careful investigation has shown that this apparently pure product is a mixture very probably of three substances, namely :—

I. Ethyl diacetyladipate =

$$\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix} CO\cdot CH_3 \\ COOC_2H_5 \end{matrix}.$$

II. Ethyl methyldihydropentene-methylketonecarboxylate* $\Big\}$ $= \begin{matrix} CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3 \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2. \end{matrix}$

III. Ethyl methyldihydropentene-dicarboxylate* ..... $\Big\}$ $= \begin{matrix} CH_3\cdot C\!=\!\!=\!\!=\!C\cdot COOC_2H_5 \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2. \end{matrix}$

* See "Nomenclature of unsaturated closed carbon chains, p. 212."

In order to separate these substances, the crude oil is dissolved in ether, and well shaken with a dilute solution of potassium hydrate, by which means a considerable quantity of a dark-coloured substance is removed. The oil is then redistilled, treated again with potassium hydrate, and the operation repeated several times until the potash has no further action on the oil.

The alkaline extract, on being acidified, deposits a quantity of a dark-brown oil, which it was found impossible to purify.

On distilling this crude substance under reduced pressure (100 mm.), carbonic anhydride is first given off and then a yellow oil distils, leaving a fairly large amount of a dark residue in the retort.

The distillate, on repeated refractionation, distils for the most part between 195° and 200° (100 mm.), and on analysis gave numbers agreeing with the formula $C_{11}H_{18}O_4$. This new substance, on hydrolysis with alcoholic potash, deposits a quantity of potassium carbonate, and yields two principal products, namely, methyldehydropentene methyl ketone and ω-acetylvalerianic acid.

These facts can be explained on the supposition that on distilling ethyl diacetyladipate, a certain amount passes over unchanged; on subsequent treatment with potassium hydrate, this is partially hydrolysed and passes into solution as potassium ethyl diacetyladipate. The free ethyl hydrogen salt, liberated by the addition of an acid, is decomposed on distillation into carbonic acid and ethyl $\alpha\omega$-diacetylvalerate, thus:—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOH\end{matrix} =$$

Ethyl hydrogen diacetyladipate.

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 + CO_2.$$

Ethyl $\alpha\omega$-diacetylvalerate.

Ethyl $\alpha\omega$-diacetylvalerate, on hydrolysis, yields ω-acetylvalerianic acid and methyldihydropentene methyl ketone, thus:—

I. $$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 + 2KOH =$$

$$CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot COOK + CH_3\cdot COOK + C_2H_5\cdot OH.$$

Potassium $\alpha\omega$-acetylvalerate.

II. $$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 + 2KOH =$$

$$CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3 \;\; (CH_2\cdot CH_2\cdot CH_2) + K_2CO_3 + C_2H_5\cdot OH + H_2O.$$

Methyldihydropentene methyl ketone.

It is very probable that this repeated fractionation and treatment

of the crude product of the distillation of ethyl diacetyladipate with potash removes other substances besides unchanged ethyl diacetyladipate; but no attempts have been made to isolate them.

The oily substance, which had been left unattacked by the potash, and which forms by far the greater portion of the whole, distilled almost constantly at 191—192° (35 mm.), and gave on analysis numbers agreeing approximately with the formula $C_{11}H_{16}O_3$.

This oil consists of two substances represented above by formulæ II and III, the latter being present in very small quantity.

On hydrolysis, this oil yields methyldihydropentene methyl ketone and small quantities of methyldihydropentenedicarboxylic acid. The former is produced from ethyl methyldihydropentenemethylketonecarboxylate, thus:—

$$\begin{matrix} CH_3\cdot C \\ \| \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} C\cdot CO\cdot CH_3 \\ | \\ \end{matrix} + 2KOH =$$

$$\begin{matrix} CH_3\cdot C \\ \| \\ CH_2\cdot CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} C\cdot CO\cdot CH_3 \\ | \\ \end{matrix} + K_2CO_3 + C_2H_5\cdot OH.$$

The latter results from the hydrolysis of ethyl methyldihydropentenedicarboxylate:—

$$\begin{matrix} CH_3\cdot C \\ \| \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} C\cdot COOC_2H_5 \\ | \\ \end{matrix} + 2KOH =$$

$$\begin{matrix} CH_3\cdot C \\ \| \\ COOK\cdot CH\cdot CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} C\cdot COOK \\ | \\ \end{matrix} + 2C_2H_5\cdot OH.$$

Methyldihydropentene methyl ketone is a colourless, mobile oil, possessing in a most pronounced manner the odour of peppermint. It boils constantly at 191° (760 mm.) and enters into a number of extremely interesting reactions, which will be fully described later on.

Methyldihydropentenedicarboxylic acid crystallises from water in large, silky needles which melt at 188°. It combines with bromine and gives Baeyer's permanganate test, and behaves in all respects like an unsaturated chain acid. When heated with hydrobromic acid, it is decomposed with evolution of carbon dioxide and formation of a neutral brominated oil, which appears to be methylbromopentamethylene—

$$\begin{matrix} CH_3\cdot C \\ \| \\ COOH\cdot CH\cdot CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} C\cdot COOH \\ | \\ \end{matrix} + HBr =$$

$$\begin{matrix} CH_3\cdot CH \\ \| \\ CH_2CH_2\cdot CH_2 \end{matrix} \begin{matrix} \\ \| \\ \end{matrix} \begin{matrix} CHBr \\ | \\ \end{matrix} + 2CO_2.$$

It is unfortunate that the amount of this acid obtained by the

above reaction is so small (1 per cent.); as, owing to its peculiar structure, many interesting results might be expected from the further study of its properties.

The hydrolysis of ethyl diacetyladipate by means of alcoholic potash has been carefully studied by Dr. Marshall and myself, and a number of interesting substances have been obtained.

If ethyl diacetyladipate is boiled only for a short time with alcoholic potash,* $\omega\omega_1$-diacetylbutane is the principal product formed, thus:—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 4KOH =$$

$$CH_3\cdot CO\cdot[CH_2]_4\cdot CO\cdot CH_3 + 2K_2CO_3 + C_2H_5\cdot OH.$$

Diacetylbutane.

This new diketone, which is the next lowest in the series to diacetylpentane, described a short time since by Dr. Kipping and myself, is a colourless crystalline mass, melting at 43—44°. It is characterised by the ease with which it loses 1 mol. H_2O with formation of methyldihydropentene methyl ketone, thus:—

$$CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 =$$

$$CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3 \;(CH_2\cdot CH_2\cdot CH_2) + H_2O.$$

this change taking place on simply boiling it with alcoholic potash.

If, therefore, ethyl diacetyladipate is boiled for some time with an excess of a strong solution of potash in alcohol, the whole of the diketone is decomposed, methyldihydropentene methyl ketone being the sole product; this reaction serving as the best method for preparing this substance. That it is identical with the methyldihydropentene methyl ketone obtained by the hydrolysis of the oil $C_{11}H_{16}O_3$, as described above, is shown by the fact that both products boil at 191° and both yield an oxime melting at 86°.

As by this method considerable quantities of the ketone could be obtained with comparative facility, numerous experiments were tried with it, with the object of obtaining data in proof of the formula $CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3$ $(CH_2\cdot CH_2\cdot CH_2)$, assigned to it throughout this paper.

When subjected to the action of excess of sodium in moist ethereal

* Prof. v. Baeyer has called my attention to the nomenclature used in these researches, and suggests that it is better to designate diketones of the formula $CH_3\cdot CO\cdot[CH_2]_n\cdot CO\cdot CH_3$ as $\omega\omega_1$-derivatives instead of $\alpha\omega$-derivatives. $\alpha\omega$-Diacetylpentane and the other similarly constituted diketones lately described by Dr. Kipping and myself should therefore be called $\omega\omega_1$-diacetylpentane, &c.

solution, this ketone, $C_8H_{12}O$, takes up 4 atoms of hydrogen and is converted into a well characterised alcohol,

$$CH_3\cdot CH\!\!-\!\!-\!\!-\!\!-CH\cdot CH(OH)\cdot CH_3,$$
$$\quad\;\; CH_2\cdot CH_2\cdot CH_2$$

which has received the name methylpentamethylene methyl carbinol.

This alcohol is a colourless oil, boiling constantly at 180°. Its acetate, $C_8H_{15}O(C_2H_3O)$, boils at 145—150° (130 mm.). Methyl pentamethylene methyl carbinol is not acted on by boiling with alcohol and excess of sodium, and it is, therefore, evidently a saturated compound. Fuming hydriodic acid converts it into its iodide, $C_8H_{15}I$, and this, when heated with fuming hydriodic acid and amorphous phosphorus at 250° for several hours, is reduced to methylethylpentamethylene (1.2),

$$\begin{array}{l} \quad\;\; CH_2 \\ \quad H_2C\quad CH_2 \\ CH_3\cdot H_2C\!\!-\!\!CH_2\cdot C_2H_5. \end{array}$$

It is a colourless oil boiling constantly at 124° and having an odour closely resembling that of the normal paraffins.

In studying these reactions one cannot but be struck with the great similarity existing between methyldihydropentene methyl ketone and the product of the internal condensation of diacetylpentane (methyltetrahydrobenzene methyl ketone), described by Dr. Kipping and myself some time since. Both these substances form oximes; both, on reduction with sodium in moist ethereal solution, take up 4 atoms of hydrogen and yield alcohols which, on treatment with hydriodic acid, are reduced to saturated hydrocarbons of the general formula C_nH_{2n}.

The arguments, based on these reactions, which were used in discussing the formula of methyltetrahydrobenzene methyl ketone (this vol., p. 14) apply equally well to the present case, and need not be again repeated. There is, however, one confirmatory test which was used in determining the constitution of methyltetrahydrobenzene methyl ketone which we have unfortunately not been able to apply to the dihydropentene-derivative. If the formula $\begin{array}{l} CH_3\cdot C\!=\!=\!=\!=C\cdot CO\cdot CH_3 \\ \quad\;\; CH_2\cdot CH_2\cdot CH_2 \end{array}$ represents the constitution of methyldihydropentene methyl ketone, it is obvious that diethyldiacetylbutane,

$$CH_3\cdot CO\cdot CH(C_2H_5)\cdot CH_2\cdot CH_2\cdot CH(C_2H_5)\cdot CO\cdot CH_3.$$

could not yield a similar condensation-product, and this fact, if demonstrated, would go far to prove the formula given above.

In order to obtain this substance, it was necessary first to prepare ethylic diethyldiacetyladipate,

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!C(C_2H_5)\cdot CH_2\cdot CH(C_2H_5)\cdot C\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix}.$$

As this compound was not formed by the action of ethylene bromide on ethyl sodioethylacetoacetate, we endeavoured to obtain it by treating the disodium compound of ethyl diacetyladipate with ethyl iodide.

The product of the reaction, on hydrolysis, gave a neutral oil, which, on fractioning first under reduced pressure and then under the ordinary pressure, distilled for the most part between 200° and 260°.

From this crude product, a substance was readily obtained boiling at 210—215°, which on analysis gave numbers agreeing with the formula $C_{10}H_{16}O$; this oil, when treated with hydroxylamine, gave an oxime $C_{10}H_{17}NO$. The general properties of the substance, and especially the strong odour of peppermint, agree so closely with those of methyldihydropentene methyl ketone that there can be no doubt that this new compound is simply the ethyl-derivative of this ketone, produced by the hydrolysis of ethylic monethyldiacetyladipate.

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!C(C_2H_5)\cdot CH_2\cdot CH_2\cdot CH_2\cdot C\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 4KOH =$$

$$\begin{matrix}CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3\\C_2H_5\cdot CH\cdot CH_2\cdot CH_2\end{matrix} + 2K_2CO_3 + 2C_2H_5\cdot OH + H_2O.$$

A second fraction, 250—255°, gave, on analysis, numbers agreeing only approximately with the formula of diethyldiacetylbutane, and owing to the very small quantity of this substance produced, we were unable to purify it further.

Some experiments were next made with the object of proving the presence of an acetyl-group in methyldihydropentene methyl ketone, as this would in a great measure confirm the formula given to this substance, and more particularly distinguish between this and the formula—

$$\begin{matrix}CH_3\cdot C\!-\!\!-\!\!-\!\!-\!\!-\!CH\\CH_2\cdot CH_2\cdot CH_2\cdot CH_2\end{matrix}\!\!>\!CO.$$

(Compare formula for methyltetrahydrobenzene methyl ketone, this vol., p. 14.) The oxime $C_8H_{13}NO$ was heated in a sealed tube with a mixture of acetic acid, acetic anhydride, and hydrogen chloride at 100° for two hours.

According to the beautiful researches of Beckmann on "intermole-

cular change in oximes," this experiment should have converted the oxime into methyldihydropenteneacetamide,

$$\begin{matrix} CH_3\cdot C & = & C\cdot NH\cdot CO\cdot CH_3 \\ | & & | \\ CH_2\cdot CH_2\cdot CH_2 & & \end{matrix},$$

a substance which on hydrolysis should have yielded methyldihydropenteneamine, $\begin{matrix} CH_3\cdot C & = & C\cdot NH_2 \\ | & & | \\ CH_2\cdot CH_2\cdot CH_2 & & \end{matrix}$, and acetic acid, as described in detail in the body of this paper.

From the product of this reaction a remarkable base was isolated, which boiled constantly at 164—165°, and volatilised readily with steam; on analysis it gave numbers agreeing with the formula $C_8H_{13}NO$, and behaved in all its reactions like a strong base. The platinochloride $(C_8H_{13}NO)_2,H_2PtCl_6$, crystallises from water in beautiful, orange-red prisms, and is very stable.

This substance is evidently not methyldihydropenteneacetamide, as even prolonged boiling with dilute hydrochloric acid does not appear to affect it, and it is thought possible that by intermolecular change the oxime has been converted into a ring-derivative having the formula—

$$CH_2<\begin{matrix} CH_2\cdot C\cdot CH_2 \\ || \\ CH_2\cdot C\cdot NH \end{matrix}>C(OH)\cdot CH_3.$$

I am at present engaged in a further study of this base.

Crude ethyl diacetyladipate, which results from distilling the product of the action of ethylene bromide on ethyl sodioacetoacetate with steam, appears to be a very fairly pure substance, as is proved not only by analysis, but also from the fact that when treated with phenylhydrazine a very large yield of phenylhydrazine-derivatives can be obtained. This is also borne out by the study of various other decompositions of this crude product, and yet, curiously enough, when treated with ammonia, even under the most varied conditions, only 30 per cent. of the theoretical yield of ethyl diimidodiethyladipate is obtained. As it was thought that this might be due to some secondary action of the ammonia, pure ethyl diacetyladipate (prepared from ethyl diimidodiethyladipate) was treated with alcoholic ammonia, with the result that over 90 per cent. of the theoretical amount of the crystalline diimido-compound was obtained.

This diimido-compound is extremely insoluble in cold alcohol, and an examination of the crude oily products contained in the mother liquors obtained by treating crude ethyl diacetyladipate with ammonia showed that it contained an imido-compound, which, however, could not be obtained in a pure state. These and other considerations

make it appear probable that crude ethyl diacetyladipate contains two structurally physical isomerides, namely :—

$$\begin{array}{c} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ | \\ [CH_2]_2 \\ | \\ CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \end{array} \quad \text{and} \quad \begin{array}{c} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ | \\ [CH_2]_2 \\ | \\ COOC_2H_5\cdot CH\cdot CO\cdot CH_3. \end{array}$$

a supposition supported to some extent by recent work on the di-substituted succinic acids.

A somewhat similar case has been noticed in studying the formation of ethyl dibenzoylsuccinate, $\begin{matrix} C_6H_5\cdot CO \\ COOC_2H_5 \end{matrix}\!>\!CH\cdot CH\!<\!\begin{matrix} CO\cdot C_6H_5 \\ COOC_2H_5 \end{matrix}$, by the action of iodine on the sodium compound of ethyl benzoylacetate. The ethereal salt usually obtained melts at 128°, but under certain conditions, which have not as yet been clearly established, an isomeric substance, m.p. 154°, results.

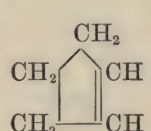
It is hoped that further investigation will clear up this interesting point.

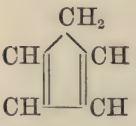
Nomenclature of Unsaturated Closed Carbon Chains.

Considerable difficulty attaches to the question of the nomenclature of partially saturated ring-derivatives, such as occur in this and the following papers.

In previous researches on the synthetical formation of closed carbon chains, only derivatives of fully saturated rings have been dealt with; such were named tri-, tetra-, penta-, hexa-methylene-derivatives, according to the number of "methylene" groups contained in the ring.

Formulæ derived from such methylene rings by the abstraction of pairs of hydrogen-atoms might be distinguished by prefixing the words dehydro-, didehydro-, tridehydro-, &c., according to the number of pairs of hydrogen-atoms removed.

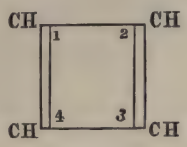
Thus the ring  would be dehydropentamethylene;

the ring  would be didehydropentamethylene, &c

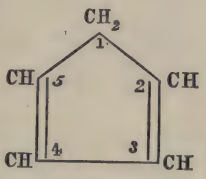
Quite apart from the inconvenient length of such words, and the difficulty of pronouncing them, the use of the word "dehydro-" in

this sense might easily cause confusion, on account of the fact that this term usually implies "elimination of water."

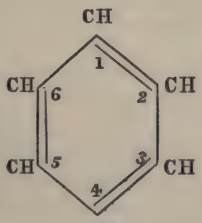
A system of nomenclature which avoids this difficulty, and which is also of general applicability, may, it seems to me, be obtained by naming the *entirely unsaturated* rings, containing *double linkings*, by following scheme, in which the position of the double linkings is shown by prefixing the sign Δ with the commencing number of the double linkings, reading in the direction of the hands of a watch, (compare Baeyer, *Annalen*, **245**, 111).



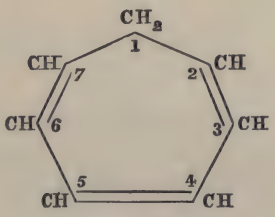
$\Delta^{2\cdot4}$-*Tetrene*.



$\Delta^{2\cdot4}$-*Pentene*.



$\Delta^{1\cdot3\cdot5}$-*Hexene* (Benzene).



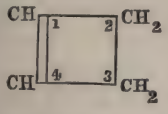
$\Delta^{2\cdot4\cdot6}$-*Heptene*.

&c.

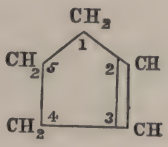
These names ending in *-ene* could not be confounded with unsaturated chain derivatives, because these have always received names ending in -ylene, such as ethylene, tetrylene, pentylene, &c.

Partially saturated derivatives of the above rings would then be named according to the number of hydrogen-atoms taken up; the position of the remaining double likings might be (as above) represented by Δ, with the number attached at which the double linking starts, counting always in the direction of the hands of a watch.

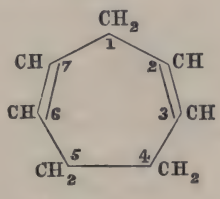
The following examples illustrate this point clearly:—



Δ^{4}-Dihydrotetrene.



Δ^{2}-Dihydropentene.

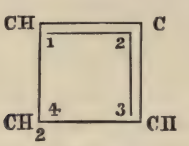


$\Delta^{2\cdot6}$-Dihydroheptene.

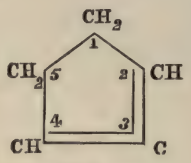
&c.

The fully saturated rings would be methylene-derivatives, as before.

Isomeric hydrocarbons, with double linkings in positions different from the above, could, if prepared, of course be similarly named, thus:—



$\Delta^{1\cdot2}$-Tetrene.



$\Delta^{2\cdot3}$-Pentene.

&c.

The substances described in this paper fall under the heading of pentene-derivatives.

$CH_3\cdot C$ (double bond) $C\cdot CO\cdot CH_3$ is Δ^2 methyldihydropentene methyl ketone (2, 3).
$CH_2\cdot CH_2\cdot CH_2$

$CH_3\cdot C$ (double bond) $C\cdot COOH$ is Δ^2 methyldihydropentenedicarboxylic acid (2, 3, 1).
$COOH\cdot CH\cdot CH_2\cdot CH_2$

&c., the numbers placed after the name in a bracket referring to the position of the side chains (Trans., 1885, **47**, 801). In most cases, where there is no fear of confusion, these numbers, as well as the symbol Δ, may be left out, as has been shown in the body of this paper.

ETHYL $\alpha_1\alpha_2$-DIACETYLADIPATE, $\frac{CH_3\cdot CO}{COOC_2H_5}>CH\cdot CH_2\cdot CH_2\cdot CH<\frac{CO\cdot CH_3}{COOC_2H_5}$.

In preparing this substance the following quantities are conveniently employed:—

Ethyl acetoacetate	260 grams.
Ethylene bromide	190 „
Sodium.....	46 „

The sodium is dissolved in 500 grams of absolute alcohol, the solution well cooled, and then the mixture of ethyl acetoacetate and ethylene bromide gradually added, the temperature being kept below 35° by repeatedly cooling with cold water. The resulting clear solution is then heated to boiling in a large flask connected with a reflux apparatus for five hours, the alcohol distilled off, sufficient water added to completely dissolve the cake of sodium bromide, and the oily layer which separates extracted three times with small quantities of ether.

The ethereal solution on evaporation deposits about 240 grams of a slightly brownish oil, which, besides ethyl diacetyladipate, contains considerable quantities of ethyl acetyltrimethylenecarboxylate, as well as unchanged ethyl acetoacetate and some ethylene bromide. In order to remove these, advantage is taken of the fact that ethyl diacetyladipate is not volatile with steam, whereas the other substances mentioned are readily carried over. The crude product is therefore submitted to rapid distillation in a current of steam, the operation being continued until no more oily drops are visible in the condensed water. The residue is extracted three times with ether, the ethereal solution washed twice with a dilute solution of sodium carbonate, dried over anhydrous potassium carbonate, filtered, and the ether distilled off.

In this way about 60 grams of a slightly brownish oil is obtained, which, after standing for some days over sulphuric acid in a vacuum, gave the following numbers on analysis:—

0·1330 gram substance gave 0·2910 gram CO_2 and 0·0920 gram H_2O.

	Theory.	Found.
C	58·74 per cent.	59·67 per cent.
H	7·69 „	7·69 „
O	33·57 „	32·64 „

Pure ethyl diacetyladipate may be readily prepared from this crude product by either of the following methods:—

I. By conversion into the disodium-derivative, and subsequent decomposition of the purified salt by dilute acids.

II. By the hydrolysis of ethyl diimidodiethyladipate.

These two methods will be given in detail in the following sections.

Disodium Compound of Ethyl Diacetyladipate,

$$\begin{matrix}CH_3{\cdot}CO\\COOC_2H_5\end{matrix}\!\!>\!CNa{\cdot}CH_2{\cdot}CH_2{\cdot}CNa\!<\!\begin{matrix}CO{\cdot}CH_3\\COOC_2H_5\end{matrix}.$$

This is best prepared in the following way:—

3·3 grams of sodium is dissolved in 30 grams of warm absolute alcohol, and the solution, while still warm, mixed with 50 grams of pure dry ether. 20 grams of crude ethyl diacetyladipate dissolved in 200 grams of pure dry ether is now added, and the yellow flocculent disodium compound, which immediately separates, rapidly filtered off, well washed with ether, and at once transferred to a vacuum desiccator.

The analysis of this compound gave the following numbers:—

I. 0·2884 gram substance gave (after ignition with H_2SO_4) 0·1190 gram Na_2SO_4.

II. 0·2605 gram substance gave (after ignition with H_2SO_4) 0·1062 gram Na_2SO_4.

	Theory. $C_{14}H_{20}Na_2O_6$.	Found. I.	Found. II.
Na	13·94 p. c.	13·37	13·23 p. c.

This disodium compound is readily soluble in alcohol, almost insoluble in ether. It is decomposed at once by dilute acids, with regeneration of ethyl diacetyladipate; water acts in the same way, but not so readily.

In preparing pure ethyl diacetyladipate, the disodium compound, after being freed from impurities by washing with ether, as explained above, is at once thrown into a considerable volume of very dilute hydrochloric acid, and the oily compound thus liberated extracted three times with pure ether. The ethereal solution, after washing with dilute sodium carbonate solution, and drying over potassium carbonate, is allowed to evaporate, when it deposits an almost colourless oil; this, after standing over sulphuric acid in a vacuum for 24 hours, was analysed with the following result:—

I. 0·2116 gram substance gave 0·4572 gram CO_2 and 0·1380 gram H_2O.

II. 0·2130 gram substance gave 0·4530 gram CO_2 and 0·1530 gram H_2O.

III. 0·1988 gram substance gave 0·4244 gram CO_2 and 0·1409 gram H_2O.

IV. 0·1226 gram substance gave 0·2632 gram CO_2 and 0·0921 gram H_2O.

	Theory.	Found. I.	Found. II.	Found. III.	Found. IV.
C	58·74	58·92	58·00	58·22	58·55
H	7·69	7·24	7·98	7·87	8·34
O.....	33·57	33·84	34·02	33·91	33·11

Ethyl diacetyladipate is a thick, colourless oil, possessing a faint, fruity odour. It does not solidify when cooled to 0°. It is miscible with ether, alcohol, and most other organic solvents, almost insoluble in water, slightly soluble in dilute aqueous solutions of potassium and sodium hydrates. The addition of a drop of ferric chloride to the alcoholic solution gives an intense violet-red coloration. When agitated for some weeks with a saturated solution of sodium hydrogen

sulphite, the ethereal salt gradually dissolves, forming a very readily soluble double compound. This, on the addition of dilute acids or carbonate of soda, deposits colourless, oily drops, which consist probably of regenerated ethyl diacetyladipate.

Ethyl diacetyladipate is readily hydrolysed by boiling with alcoholic potash, and in this way a number of interesting compounds have been obtained, which are described in the next paper.

Ethyl Diimidodiethyladipate,

$$\begin{aligned} &NH{:}(CH_3)C{<}_{COOC_2H_5}{>}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH{<}^{C(CH_3){:}NH}_{COOC_2H_5} \\ &= {}^{NH_2{\cdot}(CH_3)C}_{COOC_2H_5}{>}C{\cdot}CH_2{\cdot}CH_2{\cdot}C{<}^{C(CH_3){\cdot}NH_2}_{COOC_2H_5} \quad (?). \end{aligned}$$

This important compound is best prepared in the following way:—50 grams of crude ethyl diacetyladipate are dissolved in about 150—200 grams of absolute alcohol, and the solution thoroughly saturated with gaseous ammonia, the temperature being kept below 30° during the operation by means of cold water.

The solution on standing gradually deposits beautiful, glittering crystals, which, after 36 hours, are collected, well washed with alcohol, and dried on a porous plate.

The residual, beautifully white, glistening, crystalline mass, after recrystallisation from benzene, gave the following results on analysis:—

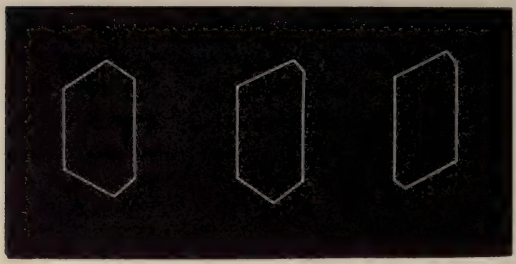
I. 0·1880 gram substance gave 0·4081 gram CO_2 and 0·1485 gram H_2O.

II. 0·1728 gram substance gave 0·3744 gram CO_2 and 0·1338 gram H_2O.

III. 0·1838 gram substance gave 16·5 c.c. N; $t = 14°$; bar. = 724 mm.

	Theory. $C_{14}H_{24}N_2O_4$.	Found. I.	II.	III.	
C	59·15 p. c.	59·20	59·09	—	p. c.
H	8·45 „	8·77	8·60	—	„
N	9·85 „	—	—	10·09	„

Ethyl diimidodiethyladipate melts at 173—174°. It is readily soluble in hot alcohol, benzene, and toluene, and crystallises from these solvents, on cooling, in beautiful, glittering plates or long, flat needles, which, when examined under the microscope, are seen to be of the following forms:—



Twin crystals were also sometimes noticed.

It is almost insoluble in water and only sparingly soluble in ether, light petroleum, or cold alcohol. Hydrochloric acid dissolves ethyl diimidodiethyladipate readily, especially on gentle warming; the addition of platinic chloride to the solution produces at first no precipitate, but on standing, glistening octahedra separate, which on examination were identified as crystals of ammonium platinochloride. This solution of ethyl diimidodiacetyladipate in hydrochloric acid remains clear for a considerable time, even when diluted with considerable quantities of water, but on gently warming on a water-bath, the liquid suddenly becomes turbid owing to the separation of minute particles of ethyl diacetyladipate, and the solution on boiling with alkalis gives off quantities of ammonia :—

$$\begin{matrix} CH_3\cdot C\cdot NH_2 & NH_2\cdot C\cdot CH_3 \\ \| & \| \\ COOC_2H_5\cdot C\cdot CH_2 & -CH_2\cdot C\cdot COOC_2H_5 \end{matrix} + 2HCl + 2H_2O =$$

$$\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\!\begin{matrix} CO\cdot CH_3 \\ COOC_2H_5 \end{matrix} + 2NH_4Cl.$$

This decomposition serves as a ready means of preparing pure ethyl diacetyladipate from the crude product, without the necessity of using the disodium compound. For this purpose the finely-divided diimido-compound is agitated with just sufficient hydrochloric acid (sp. gr. 1·16) to dissolve it, the clear solution diluted with 3 vols. of water and warmed on a water-bath to about 80°. Long before the solution attains this temperature a cloudiness suddenly appears, and in a short time a thick, oily layer of ethyl diacetyladipate settles down in the aqueous solution.

This is extracted twice with pure ether, the ethereal solution washed with sodium carbonate, dried over potassium carbonate, and evaporated. The resulting colourless oil, after standing for some hours over sulphuric acid in a vacuum, consists of pure ethyl diacetyladipate, as the following analysis shows :—

0·1505 gram substance gave 0·1046 gram H_2O and 0·3228 gram CO_2.

	Theory. $C_{14}H_{22}O_6$.	Found.
C	58·74 per cent.	58·49 per cent.
H	7·69 „	7·72 „
O	33·56 „	33·79 „

This method is the most convenient for preparing pure ethyl diacetyladipate, although the yield obtained is only 30 per cent. of the crude product employed.

In preparing ethyl diimidodiethyladipate, as described above, rarely more than 30 per cent. of the crystalline substance is obtained, notwithstanding that the ethyl diacetyladipate employed could have contained only a small quantity of impurity, as shown by the yields of other derivatives obtained from it.

The mother liquors from the crystals were found on examination to contain a large quantity of an oily ammonium compound which could not be obtained in a pure state. In order, if possible, to improve the yield of ethyl diimidodiethyladipate, various experiments were tried, using not only different solvents, but also varying quantities of ammonia, but without success. If crude ethyl diacetyladipate is shaken with an excess of strong aqueous ammonia, and the solution allowed to stand for some days, the globules of oil gradually become more and more viscid and at last break up entirely into semi-solid particles. These are collected, freed from oil by spreading on a porous plate, and washed with alcohol. The colourless crystalline mass thus obtained is identical with the substance described above, and the yield is almost the same as that obtained with alcoholic ammonia.

As the yield of crystals by all methods was so small, it seemed probable that the ammonia exerted some secondary influence on the ethyl diacetyladipate, converting it possibly into an acid amide. In order to test this, 5 grams of pure ethyl diacetyladipate (prepared from ethyl diimidodiethyladipate) was dissolved in 20 grams of pure methyl alcohol, the solution saturated with ammonia and allowed to stand for 24 hours. The crystals of the diimido-compound thus formed were collected, washed with alcohol, and found to weigh 4·1 grams. The mother liquor, on evaporation at the ordinary temperature, deposited 0·53 gram of crystals, but no trace of an oily ammonia compound had been formed. The yield obtained was therefore about 93 per cent. of the theoretical.

The obvious conclusion to be drawn from these facts is that crude ethyl diacetyladipate contains two structurally isomeric substances, one of which gives a crystalline, the other an oily diimido-, compound. It has not as yet been possible to prove this supposition, but further experiments on the subject are in progress.

Action of Phenylhydrazine on Ethyl Diacetyladipate.

Ethyl diacetyladipate reacts very readily with phenylhydrazine, giving rise to well-characterised products, the formation of which proves beyond doubt that this substance really has the constitution assigned to it in this paper.

If equal volumes of crude ethyl diacetyladipate and phenylhydrazine are mixed together, a considerable rise of temperature takes place, and in a short time the mixture becomes cloudy, owing to the separation of water. This product, when heated on a water-bath, soon separates into two layers, and on prolonged heating, the whole solidifies to a crystalline cake. In order to purify this crude substance, the mass is first ground up in a mortar with ether, filtered from the dark-brown ethereal solution, the residue washed with ether till colourless, and then dried by spreading it on a porous plate. The colourless crystalline mass thus obtained is a mixture of two substances, one of which is soluble in methyl alcohol, the other insoluble.

In order to separate these, the crystalline powder is extracted two or three times with boiling methyl alcohol, filtered, and the solution concentrated and allowed to stand. In a short time ethyl diphenylhydrazinediacetyladipate separates in faintly yellowish plates, which after drying first on a porous plate and then over sulphuric acid in a vacuum, gave the following results on analysis.

I. 0·2191 gram substance gave 0·5374 gram CO_2 and 0·1480 gram H_2O.

II. 0·1615 gram substance gave 18 c.c. N; $t = 20°$; bar. = 720 mm.

	Theory. $C_{26}H_{34}N_4O_4$.	Found. I.	Found. II.	
C	66·95 per cent.	66·89	—	per cent.
H	7·30 „	7·50	—	„
N.....	12·02 „	—	12·06	„

This substance is formed by the union of 1 mol. of ethyl diacetyladipate with 2 mols. of phenylhydrazine, with elimination of 2 mols. H_2O, thus:—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}>CH\cdot CH_2\cdot CH_2\cdot CH<\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 2C_6H_5\cdot NH\cdot NH_2 =$$

$$\begin{matrix}CH_3\cdot C(N_2H\cdot C_6H_5)\\COOC_2H_5\end{matrix}>CH\cdot CH_2\cdot CH_2\cdot CH<\begin{matrix}C(N_2H\cdot C_6H_5)\cdot CH_3\\COOC_2H_5\end{matrix} + 2H_2O.$$

Ethyl diphenylhydrazinediacetyladipate melts at about 143—145°, but when heated above this point decomposition sets in very rapidly; at

200°, the mass again becomes solid, owing to its conversion into bis-phenylmethylmethylenepyrazolone (see below).

It is readily soluble in strong acids, but insoluble in alkalis. It dissolves moderately easily in boiling methyl alcohol, but only very sparingly in ether, toluene, ethyl acetate, chloroform, acetone, or light petroleum in the cold. From its solution in hot methyl or ethyl alcohol, it crystallises on slowly cooling in thin, colourless four-sided plates or long, slender needles.

The second substance which is formed when ethyl diacetyladipate and phenyhyldrazine react, and which remains as a white powder after extracting the ethyl diphenylhydrazinediacetyladipate by boiling methyl alcohol as described above, is best purified by recrystallisation from dilute acetic acid. For this purpose the substance is dissolved in boiling acetic acid, the hot liquid filtered, and water added until a very slight turbidity is produced. The solution, on standing, then deposits the new compound in colourless, prismatic crystals, which, after collecting, washing first with dilute acetic acid and then with water, and drying at 130°, gave the following results on analysis:—

I. 0·1537 gram substance gave 0·3960 gram CO_2 and 0·0853 gram H_2O.

II. 0·2830 gram substance gave 37·5 c.c. N; $t = 10°$; bar. = 722 mm.

	Theory. $C_{22}H_{22}N_4O_2$.	Found. I.	Found. II.	
C	70·58 per cent.	70·26	—	per cent.
H	5·88 ,,	6·16	—	,,
N	14·97 ,,	—	15·06	,,

This substance is formed from ethyl diphenylhydrazinediacetyladipate by elimination of two molecules of alcohol, thus:—

$$CH_3\cdot C(N_2HC_6H_5)(COOC_2H_5)>CH\cdot CH_2\cdot CH_2\cdot CH<C(N_2HC_6H_5)\cdot CH_3(COOC_2H_5) =$$

$$C_6H_5\cdot N<CO\cdot CH\cdot CH_2\cdot CH_2\cdot HC\cdot CO\,(N=C\cdot CH_3)\,(CH_3\cdot C=N)>N\cdot C_6H_5 + 2C_2H_5\cdot OH.$$

and is, therefore, bis-1-phenyl-3-methyl-4-methylene-5-pyrazolone. It is almost insoluble in neutral organic solvents, but readily soluble in acetic acid. From dilute acetic acid it separates in colourless, prismatic crystals, which do not melt at 250°.

This pyrazolone is readily soluble both in acids and alkalis. If the pure substance be warmed with moderately dilute hydrochloric acid,

it dissolves readily, forming a colourless solution, which on cooling deposits the salt, either as a gelatinous mass or in the form of microscopic needles, according to whether the solution was strong or weak. The gelatinous precipitate, on rubbing or warming gently, at once becomes crystalline. On boiling the hydrochloric solution with either ferric or platinic chlorides, a white, sparingly soluble crystalline substance is precipitated, which is possibly an oxidation-product. Warm dilute sulphuric acid also dissolves the pyrazolone readily; on cooling the solution sets to a transparent jelly, which, on rubbing, eventually becomes crystalline, although not so readily as the hydrochloride. A delicate test, which seems to show the presence of very small quantities of this substance, is the following:—A trace of the pyrazolone is gently boiled with concentrated nitric acid, until the oxidation, which sets in at once, is complete (after about two minutes). The resulting, almost colourless solution, on the addition of a few drops of water, deposits a yellow, crystalline substance, which dissolves in potassium hydrate, forming an intensely reddish-brown liquid.

Bis-phenylmethylmethylenepyrazolone combines very readily with alkalis. The potassium salt was obtained as follows:—The substance was dissolved in a little warm potassium hydrate (sp. gr. 1·2), and then mixed with a concentrated solution of the alkali (sp. gr. 1·4), until a decided precipitate was obtained. This dissolved on boiling, and on allowing the solution to cool slowly, the potassium salt crystallised out in large, transparent, flaky crystals. These were collected, washed four or five times with small quantities of water, and freed from mother liquor as completely as possible by spreading on a porous plate. The resulting satiny crystals dissolved in water very readily, producing a faintly alkaline solution, which showed the following behaviour with precipitants:—*Copper sulphate.*—A pinkish-white precipitate, very sparingly soluble even in boiling water. *Cadmium chloride.*—A heavy white, crystalline precipitate, very sparingly soluble in water. *Silver nitrate.*—A white, gelatinous precipitate, which on boiling turned black. *Uranium nitrate.*—An orange-white precipitate, resembling ferric benzoate in appearance.

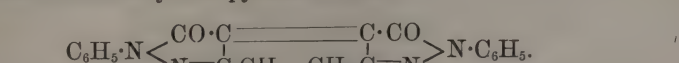
From the study of these properties it is at once evident that a great similarity exists between this substance and bis-phenylmethylpyrazolone:—

$$C_6H_5\cdot N<\begin{matrix}CO\cdot CH & HC\cdot CO\\ \|\ \ \ & \ \ \ |\\ N=C\cdot CH_3 & CH_3\cdot C=N\end{matrix}>NC_6H_5.$$

which Knorr (*Ber.*, **17**, 2050) obtained by the action of phenylhydrazine on ethyl diacetylsuccinate.

There is, however, one characteristic difference between these two

substances, bis-phenylmethylpyrazolone on oxidation with ferric or platinic chlorides yields pyrazole-blue:—



Knorr, (*Annalen*, **238**, 171), whilst bis-phenylmethylmethylenepyrazolone, as might be expected from an examination of its constitution, yields no trace of colouring matter when subjected to similar treatment.

If, however, a solution of the substance in dilute hydrochloric acid is boiled with excess of ferric chloride, a crystalline precipitate is soon produced; this is deposited from its solution in hot dilute acetic acid as a sandy crystalline mass, insoluble in alkalis. It was not analysed.

Decomposition of Ethyl Diacetyladipate by Heat.

In studying this interesting decomposition, crude ethyl diacetyladipate in quantities of 15 grams at a time, was first submitted to rapid distillation under reduced pressure (225 mm.) from retorts not fitted with thermometers. A large quantity of a slightly yellowish oil distilled over, leaving a considerable carbonaceous residue in the retorts. The distillation from several such operations was next very carefully fractioned under 225 mm. pressure. Below 180° a small quantity of ethyl acetyltrimethylenecarboxylate passed over; then the thermometer rose rapidly to 200°, between which temperature and 240° the greater part distilled as a yellowish oil, leaving a small residue in the retort which was not further examined.

On repeatedly fractioning this distillate under the same pressure, a considerable quantity of an almost colourless oil was obtained, which boiled fairly constantly at 230—231°. This oil on analysis gave the following numbers, each analysis being made from a different preparation.

I. 0·2165 gram substance gave 0·5013 gram CO_2 and 0·1553 gram H_2O.

II. 0·1947 gram substance gave 0·4483 gram CO_2 and 0·1342 gram H_2O.

III. 0·1522 gram substance gave 0·3504 gram CO_2 and 0·1092 gram H_2O.

IV. 0·1669 gram substance gave 0·3859 gram CO_2 and 0·1164 gram H_2O.

	Theory for $C_{14}H_{20}O_5$.	Found. I.	II.	III.	IV.
C.....	62·68 p. c.	63·15	62·74	62·79	63·03 p. c.
H.....	7·47 „	7·96	7·66	7·97	7·74 „
O.....	29·84 „	28·89	29·60	29·24	29·23 „

From this result the conclusion was at once drawn that the substance is formed simply by the elimination of 1 mol. H_2O from 1 mol. ethyl diacetyladipate, thus:—

$$C_{14}H_{22}O_6 = C_{14}H_{20}O_5 + H_2O.$$

Subsequent experiments showed that, in spite of its constant boiling-point, it was a mixture of at least three compounds, and this rendered a very careful reinvestigation of this product very desirable. A large quantity of crude ethyl diacetyladipate which had accumulated as a bye-product from various researches, was submitted to distillation under a pressure of 160 mm. The crude, oily distillate was carefully fractioned, and all passing over between 200—225° (160 mm.) collected apart. This oil, which on analysis gave numbers closely agreeing with those obtained above, was dissolved in five times its bulk of ether, and thoroughly agitated with a small quantity of a moderately dilute solution of potassium hydrate, the aqueous layer was separated, and the operation repeated until the potash solution was coloured slightly yellow only. The alkaline solutions were carefully preserved and investigated in the way to be explained later. The ethereal solution was dried over anhydrous potassium carbonate, the ether distilled off, and the resulting oily residue submitted to very careful fractionation under a pressure of 170 mm. In this way a slightly yellowish oil was obtained, boiling constantly at 215—217° (170 mm.), which on analysis gave the following numbers:—

I. 0·1549 gram substance gave 0·1170 gram H_2O and 0·3720 gram CO_2

II. 0·1544 gram substance gave 0·1189 gram H_2O and 0·3698 gram CO_2.

	Found. I.	II.
C.....	65·49	65·32 per cent.
H.....	8·39	8·55 „
O.....	26·12	26·13 „

As this operation had evidently removed a considerable quantity of a substance containing a lower percentage of carbon than the principal constituent of the oil, it was thought that if the treatment with potash were repeated, a pure product might be obtained. The oil was therefore again dissolved in ether, and the agitation with

potash continued until the alkali apparently had no further action on it.

The product, after two or three fractionations, distilled very constantly at 215—217° (167 mm.), and gave the following numbers on analysis:—

I. 0·1947 gram substance gave 0·1465 gram H_2O and 0·4718 gram CO_2.

II. 0·1710 gram substance gave 0·1250 gram H_2O and 0·4140 gram CO_2.

	Found. I.	II.
C	66·04	66·02 per cent.
H	8·36	8·12 ,,
O	25·60	25·86 ,,

As this result was still considered unsatisfactory, the treatment with potash was twice more repeated, the oil being redistilled between each operation. The resulting, almost colourless oil passed over for the most part at 191—192° (35 mm.). Analysis:—

I. 0·2220 gram substance gave 0·1640 gram H_2O and 0·5450 gram CO_2.

II. 0·1919 gram substance gave 0·1433 gram H_2O and 0·4730 gram CO_2.

III. 0·1756 gram substance gave 0·1285 gram H_2O and 0·4320 gram CO_2.

	Theory. $C_{11}H_{16}O_3$.	Found. I.	II.	III.
C	67·34	66·95	67·22	67·09 p. c.
H	8·16	8·20	8·29	8·13 ,,
O	24·49	24·85	24·59	24·78 ,,

Further treatment with potash had practically no effect on the ethereal solution of this substance, as the product boiled at the same temperature, and gave on analysis C = 67·28, H = 8·21.

In order to test further the composition of this oil, its molecular weight was determined in acetic acid solution by Raoult's method with the following result:—

Weight of substance	1·2680 grams.
Weight of acetic acid	51·07 ,,
M. p. of acetic acid	14·76°
M. p. of mixture	14·27°
Depression of m. p.	0·49°

Mol. wt. $C_{11}H_{16}O_3$.	Found.
196	197

Although this substance boils so constantly, it is evident from the study of its decomposition on hydrolysis (see p. 231) that it must consist of two compounds, having their boiling points either identical or lying very near to one another; the second substance being present in very small quantity only.

I. Ethyl methyldihydropentene-methylketonecarboxylate.. $\left.\begin{array}{l} CH_3\cdot C \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2 \end{array}\right\} C\cdot CO\cdot CH_3$

II. Ethyl methyldihydropentene-dicarboxylate..... $\left.\begin{array}{l} CH_3\cdot C \\ COOC_2H_5\cdot CH\cdot CH_2\cdot CH_2 \end{array}\right\} C\cdot COOC_2H_5.$

This oil is almost colourless, has a disagreeable odour, and does not solidify when cooled to 0°. It is almost insoluble in water, but readily soluble in alcohol, ether, and most other organic solvents.

Its alcoholic solution does not give any coloration with ferric chloride, although the crude oil before treatment with potash gives an intense violet coloration.

It next appeared interesting to determine the nature of the substance which had been removed by the alkali in the purification of the oil $C_{11}H_{16}O_3$, as described above.

During this operation, each small amount of potash which was used was at once run into a large bottle containing excess of dilute sulphuric acid, in order that the excess of potash might have no further effect on the dissolved oil. The combined extracts were extracted three times with ether, the ethereal solution washed once with water, dried over calcium chloride, and evaporated; in this way a considerable quantity of a dark-brown oil was obtained, which, in alcoholic solution, gave an intense violet coloration with ferric chloride.

As this oil could not be made to crystallise, it was thought that some idea as to its constitution might be obtained on examining the products formed on distillation under reduced pressure. On gently heating in a fractionation flask (under a pressure of 100 mm.), decomposition rapidly set in with abundant evolution of carbon dioxide, and as the temperature rose a yellow oil distilled without further decomposition. The oily distillate was mixed with ether, extracted twice with dilute potash, to remove acid substances, and then repeatedly fractioned under a pressure of 100 mm. In this way a colourless oil was obtained boiling at 195—200° (100 mm.), which, on analysis, gave the following numbers:—

I. 0·1840 gram substance gave 0·1402 gram H_2O and 0·4150 gram CO_2.

II. 0·1650 gram substance gave 0·1248 gram H_2O and 0·3740 gram CO_2.

	Theory. $C_{11}H_{18}O_4$.	Found. I.	Found. II.
C	61·68 per cent.	61·45	61·81 per cent.
H.....	8·41 „	8·47	8·28 „
O.....	29·90 „	30·08	29·91 „

This new compound is a colourless oil, readily soluble in ether and alcohol, sparingly soluble in water. Its alcoholic solution gives a violet coloration with ferric chloride. A clear insight into the constitution of this oil is obtained from the study of its behaviour on hydrolysis, when it is decomposed into acetovaleric acid, acetic acid, and small quantities of methyldihydropentene methyl ketone (see page 229). This behaviour can only be explained on the assumption that the substance is ethyl $\alpha\omega$-diacetylvalerate,

$$\begin{array}{l} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ \qquad\quad | \\ \qquad\quad CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3, \end{array}$$

a compound which would readily be formed by the distillation of ethyl hydrogen diacetyladipate, thus:—

$$\begin{array}{l} CH_3\cdot CO \\ COOC_2H_5 \end{array}\!\!>\!CH\cdot CH_2\cdot CH_2\!<\!\begin{array}{l} CO\cdot CH_3 \\ COOH \end{array} =$$

$$\begin{array}{l} CH_3\cdot CO \\ COOC_2H_5 \end{array}\!\!>\!CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3 + CO_2.$$

The formation of ethyl hydrogen diacetyladipate can be explained on the supposition that the crude product of the distillation of ethyl diacetyladipate still contains some unchanged substance, and that this, on shaking with potash, is partially hydrolysed, and passes into solution as ethyl potassium diacetyladipate.

In order to test this supposition, some crude ethyl diacetyladipate was dissolved in ether and repeatedly agitated with dilute potash solution. The slightly brownish extract was run into dilute sulphuric acid, the resulting turbid solution extracted with ether, and the ethereal solution again agitated with very dilute potash solution. The alkaline liquid, on acidifying, deposited yellowish oily drops, which were extracted with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a considerable quantity of a thick, brownish oil. This oil was completely soluble in sodium carbonate solution; its alcoholic solution gave an intense violet coloration with ferric chloride, and on heating in a small Würtz flask it readily decomposed with evolution of carbon dioxide, and formation of a slightly yellowish, neutral oil, which also gave the violet coloration with ferric chloride. These reactions are exactly similar to those of the oil which was deposited on acidifying the

alkaline extract of the product of the distillation of ethyl diacetyladipate, and this experiment tends to strengthen the view of the formation of ethyl diacetylvalerate given above. That the crude substance obtained as described above was in reality ethyl hydrogen diacetyladipate is rendered the more probable by the results of the following analysis of a sample of the crude product, which had been dried over sulphuric acid in a vacuum for 24 hours :—

0·1171 gram substance gave 0·2420 gram CO_2 and 0·0736 gram H_2O.

	Theory. $C_{12}H_{18}O_6$.	Found.
C	55·81 per cent.	56·36 per cent.
H	6·97 „	6·99 „
O	37·21 „	36·65 „

Hydrolysis of Ethyl Diacetylvalerate.

In studying this decomposition, crude ethyl diacetylvalerate (b. p. 190—210° under 100 mm.) was mixed with an excess of a strong solution of potash in methyl alcohol, and gently boiled on a water-bath in a flask connected with a reflux apparatus. Hydrolysis set in rapidly, the liquid became brownish-coloured, and a quantity of potassium carbonate separated. At the end of two hours the alcohol was distilled off, water added, and the alkaline liquid, which smelt strongly of peppermint, extracted twice with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a small quantity of an oil which smelt strongly of peppermint, and which, on distillation, passed over for the most part between 185° and 200°, and possessed all the properties of methyldihydropentene methyl ketone.

The alkaline solution was evaporated on a water-bath till free from alcohol, mixed with a considerable quantity of water, and acidified with dilute sulphuric acid. The small quantity of a dark-brownish, resinous mass thus precipitated was filtered off, and the clear filtrate extracted repeatedly with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a quantity of a brownish oil which smelt very strongly of acetic acid.

On purifying this by fractionating under reduced pressure (280 mm.), a small quantity of a very acid liquid passed over below 120°, which was readily recognised as acetic acid; then the thermometer rose rapidly to 240°, between which temperature and 260° the greater part distilled. On refractioning, an oil was obtained boiling at 250—253° (280 mm.) which, when cooled in a freezing mixture, solidified to a mass of crystals. These were freed from oily impurities

by spreading on a porous plate, remelted, allowed to solidify, again spread on a porous plate, and the colourless crystals thus obtained dried over sulphuric acid, and analysed with the following result:—

0·1792 gram substance gave 0·1378 gram H_2O and 0·3820 gram CO_2.

	Theory. $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}COOH$.	Found.
C	58·33 per cent.	58·14 per cent.
H	8·33 „	8·54 „
O	33·33 „	33·32 „

Acetovaleric acid thus purified melts at 40—42°, and when heated in small quantities appears to distil at the ordinary pressure without decomposition. It is readily soluble in water, alcohol, ether, and most other organic solvents. Its aqueous solution has a decidedly acid reaction, and gives with phenylhydrazine acetate, after a short time, a precipitate of an oily phenylhydrazine compound.

Acetovaleric acid, which is isomeric with α-ethyl-β-acetopropionic acid, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(C_2H_5){\cdot}COOH$, completes the series of ω-acetocarboxylic acids up to C_9, thus:—

	M. p.
Pyruvic acid, $CH_3{\cdot}CO{\cdot}COOH$.....	Oil
Acetoacetic acid, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOH$.....	Oil
Levulinic acid, $CH_3{\cdot}CO{\cdot}[CH_2]_2{\cdot}COOH$.....	33°
ω-Acetobutyric acid, $CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}COOH$..	Oil
ω-Acetovaleric acid, $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}COOH$ ..	40–42°
ω-Acetocaproic acid, $CH_3{\cdot}CO{\cdot}[CH_2]_5{\cdot}COOH$.	30°

Salts of Acetovaleric Acid.

The salts of this acid are mostly soluble in water. For the following experiments, an aqueous solution of the acid was exactly neutralised with ammonia, and the resulting solution of the very readily soluble ammonium salt employed. *Silver nitrate* gives a white, crystalline precipitate which dissolves readily in boiling water, and crystallises out on cooling in beautiful, colourless, leafy masses. For analysis, the salt was collected, well washed with water, and dried over sulphuric acid in a vacuum.

I. 0·2516 gram substance gave 0·0980 gram H_2O, 0·3054 gram CO_2, and 0·1082 gram silver.

II. 0·2032 gram substance gave 0·0780 gram H_2O, 0·2476 gram CO_2, and 0·0875 gram silver.

III. 0·2596 gram substance gave 0·1117 gram silver.

	Theory. $C_7H_{11}AgO_3$.	Found. I.	II.	III.	
C	33·46 p. c.	33·10	33·23	—	p. c.
H	4·38 „	4·33	4·26	—	„
Ag	43·04 „	43·00	43·06	43·02	„

This silver salt is very stable, and not readily affected by light.

Copper sulphate gives no precipitate when mixed with a moderately dilute solution of the ammonium salt. On boiling, however, a greenish-white precipitate separates, which has a crystalline appearance. When examined under the microscope, it was found to consist of a mass of minute, transparent spherules.

Hydrolysis of the Oil $C_{11}H_{16}O_3$.

In order to obtain some clue as to the constitution of this oil, its behaviour when treated with alcoholic potash was next very carefully investigated.

52 grams of the oil (1 mol.) was dissolved in a little methyl alcohol, heated to boiling in a flask connected with a reflux apparatus, and a solution of 40 grams of pure potash (4 mols.) in methyl alcohol run in drop by drop. During this operation, which occupied about half-an hour, the solution became brownish and deposited a quantity of potassium carbonate; as soon as all the potash solution had been run in, the alcohol was quickly distilled off, and the dark-coloured oil which was precipitated on the addition of water extracted three times with ether. The ethereal solution, after well washing with water, drying over potassium carbonate, and evaporating, deposited 19 grams of a dark-coloured oil, which, on fractionating, distilled for the most part between 180° and 210°, leaving, however, a considerable quantity of a thick, oily residue of high boiling point in the retort. After repeated fractioning in a Würtz flask, provided with a long neck, 8 grams of oil were obtained boiling constantly at 191—191·5° (Analysis I).

Analyses II and III were made with a different preparation which boiled at 188—190° (720 mm.).

I. 0·1680 gram substance gave 0·1473 gram H_2O and 0·4771 gram CO_2.

II. 0·1868 gram substance gave 0·1665 gram H_2O and 0·5293 gram CO_2.

III. 0·1668 gram substance gave 0·1458 gram H_2O and 0·4709 gram CO_2.

	Theory. $C_8H_{12}O$.	Found. I.	II.	III.
C	77·42 p. c.	77·39	77·22	76·91 p. c.
H	9·68 „	9·74	9·90	9·72 „
O	12·90 „	12·87	12·88	13·37 „

This substance is a colourless, very volatile oil, possessing a penetrating odour of peppermint. It is readily soluble in most organic solvents, insoluble in and lighter than water. It combines readily with phenylhydrazine and with hydroxylamine, forming in the former case an oily hydrazine compound, in the latter case a beautifully crystalline oxime.

This interesting substance, $C_8H_{12}O$, is identical with the compound produced by the action of dehydrating agents on $\omega\omega_1$-diacetylbutane (see next paper).

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3 = C_8H_{12}O + H_2O.$$

When treated with reducing agents, it takes up 4 atoms of hydrogen and is converted into an alcohol, $C_8H_{16}O$, and this on treatment with hydrogen iodide at 250° yields the hydrocarbon C_8H_{16}.

Arguing from these and other decompositions, which have been fully explained in the introduction, it is probable that the constitution of this substance is represented by the formula—

$$CH_3{\cdot}C\!=\!\!=\!\!=\!\!=\!\!=C{\cdot}CO{\cdot}CH_3 \quad ,$$
$$\quad\quad\quad

well washed with hot water. The filtered solution was acidified with hydrochloric acid, extracted 10 times with ether, the ether evaporated, and the residual oil treated a second time with baryta-water, and again extracted. The resulting yellowish oil was boiled with 1 litre of water, filtered from a little dark coloured insoluble matter, and repeatedly extracted with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited about 12 grams of a yellowish oil; this, on being allowed to remain for some days over sulphuric acid in a vacuum, deposited crystals, but did not entirely solidify.

The crystals were roughly freed from oily mother liquor by means of a vacuum filter, and the yellowish semi-solid mass spread on a porous plate and allowed to stand for two weeks. The resulting, almost colourless, crystalline product was then readily purified by recrystallisation from water, with the aid of a little animal charcoal; in this way, beautiful glittering needles were obtained, which, after drying at 100°, gave the following results, on analysis:—

I. 0·1231 gram substance gave 0·0676 gram H_2O and 0·2560 gram CO_2.

II. 0·1843 gram substance gave 0·0894 gram H_2O and 0·3848 gram CO_2.

III. 0·1540 gram substance gave 0·0845 gram H_2O and 0·3180 gram CO_2.

	Theory. $CH_3{\cdot}C{=\!=\!=}C{\cdot}COOH$ $COOH{\cdot}CH{\cdot}CH_2{\cdot}CH_2$	Found. I.	II.	III.
C	56·47 p. c.	56·71	56·94	56·31 p. c.
H	5·88 „	6·04	5·39	6·09 „
O	37·65 „	37·25	37·67	37·60 „

Methyldihydropentenedicarboxylic acid melts at 188°. It is readily soluble in hot water, alcohol, and acetone, but only sparingly in cold light petroleum, benzene, carbon bisulphide, and chloroform. This acid usually crystallises from water in long, thin, colourless prisms, but on several occasions thick groups of plates have been obtained which are very different from the needle-shaped crystals. If the needles be dissolved in boiling water, the solution crystallises very rapidly on cooling, whereas the hot solution of the plates takes one or two hours to crystallise. Both forms give the same melting point, and the same results on analysis, but I have not yet succeeded in obtaining the needles from the plates or *vice versâ*.

Salts of Methyldihydropentenedicarboxylic Acid.

Ammonium Salt.—In preparing this salt the pure acid was dissolved in a little hot water, the solution rendered slightly alkaline by the addition of ammonia, and allowed to cool over sulphuric acid in a vacuum. This salt is extremely soluble in water, and if the solution is allowed to evaporate over sulphuric acid, a gelatinous residue is obtained.

Normal Silver Salt, $C_8H_8O_4Ag_2$.—If silver nitrate in considerable excess is added to a faintly alkaline solution of the ammonium salt, a heavy white precipitate of the normal silver salt is thrown down. This was collected, washed with a little warm water, and dried over sulphuric acid in a vacuum. Analysis:—

I. 0·1579 gram substance gave 0·0355 gram H_2O and 0·1450 gram CO_2.

I*a*. 0·1438 gram substance gave 0·0801 gram Ag.

	Theory. $C_8H_8O_4Ag_2$.	Found.
C	25·00 per cent.	24·89 per cent.
H	2·09 „	2·49 „
Ag	56·25 „	55·70 „

This salt darkens very readily when exposed to light. When heated it decomposes all at once, giving a very voluminous mass of carbon and silver.

Hydrogen Silver Salt, $C_8H_9O_4Ag$.—In preparing a quantity of the normal silver salt for some experiments, the mother liquors on standing deposited a considerable crop of fine needles. These were collected, washed with a little water, dried over sulphuric acid, and analysed with the following results:—

0·2001 gram substance gave 0·0594 gram H_2O, 0·254 gram CO_2, and 0·0798 gram Ag.

	Theory. $C_8H_9O_4Ag$.	Found.
C	34·66 per cent.	34·22 per cent.
H	3·25 „	3·29 „
Ag	38·99 „	39·88 „

This salt is readily soluble in hot water. The solution on cooling deposits a mass of very slender needles. The same salt may be obtained by adding nitrate of silver to a dilute neutral solution of the ammonium salt, filtering off the slight precipitate which forms, and allowing the solution to stand in a dark place; after some time fine needles of the hydrogen silver salt separate. The tendency to form

this salt, even in neutral solutions, is so great that it was found extremely difficult to prepare a specimen of normal salt pure enough to give good numbers on analysis, most of the analyses showing a deficiency of 1 to 1·5 per cent. Ag.

A neutral solution of the ammonium salt shows the following behaviour with reagents:—*Copper sulphate* gives a deep, bluish-green precipitate, which is very sparingly soluble even in boiling water. *Lead acetate* gives only a slight precipitate in the cold; on warming, the solution becomes turbid and a white amorphous salt separates, which, however, dissolves again on cooling. *Cadmium chloride* gives no precipitate.

The following experiments were conducted with the small quantity of acid at my disposal.

Action of Bromine on Methyldihydropentenedicarboxylic Acid.

A solution of the pure acid in glacial acetic acid seems not to be acted on by bromine even on warming. If, however, an aqueous solution of the acid is mixed with bromine water, decolorisation takes place in the cold. On evaporating the solution, a syrupy residue is obtained, which when warmed, rapidly turns black and gives off hydrogen bromide. It was also found that when the acid was first converted into the chloride by means of PCl_5, and then treated with bromine (as recommended by Baeyer (*Annalen*, **245**, 162), that addition took place at once; but, in spite of several attempts, the dibrominated acid could not be obtained in the crystalline condition.

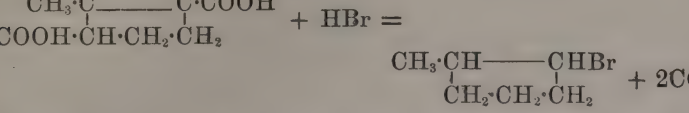
Action of Hydrobromic Acid on the Acid.

Two grams of the pure acid were heated with 14 c.c. of hydrobromic acid (sp. gr. 1·65) in a sealed tube for 4 hours at 100° and then for 3 hours at 120°. On opening the tube much carbon dioxide escaped, and the product on examination was found to consist of an almost colourless liquid in which light-brown, oily drops were suspended. The whole was extracted with ether, the ethereal solution rapidly washed, dried over calcium chloride, and the ether evaporated. The residual, light-brown oil, which weighed 1·3 gram, was placed over sulphuric acid in a vacuum, and then analysed with the following result:—

0·1907 gram substance, heated at 180° for 4 hours with fuming nitric acid, gave on precipitation with $AgNO_3$, 0·2164 gram AgBr.

	Theory. $C_6H_{11}Br$.	Found.
Br	49·08 per cent.	48·22 per cent.

It is extremely probable that this substance is methylbromopentanethylene, formed according to the equation—



The substance was a brownish oil, having an odour somewhat resembling that of trimethylene bromide. On standing, it became darker and darker, and ultimately almost black, considerable quantities of hydrogen bromide being evolved.

Action of Sodium Amalgam on the Acid.

Two grams of the pure acid were dissolved in a little sodium carbonate, and gradually mixed with 250 grams of 3 per cent. sodium amalgam. The product was filtered, acidified with sulphuric acid, the precipitate collected, and recrystallised from water. In this way beautiful colourless needles were obtained which melted at 188°, and possessed all the properties of the original acid. The analysis showed that no addition of hydrogen had taken place:—

0·1446 gram substance gave 0·0762 gram H_2O and 0·2996 gram CO_2.

	Theory. $C_8H_{10}O_4$.	Found.
C	56·47 per cent.	56·57 per cent.
H	5·88 „	5·85 „
O	37·65 „	37·58 „

Further experiments on the action of reducing agents on this acid are in progress.

METHYLDIHYDROPENTENEMETHYLKETONEOXIME.

In order to prove the ketonic nature of methyldihydropentene methyl ketone, its behaviour towards hydroxylamine was carefully studied.

Six grams of the pure substance dissolved in a little methyl alcohol was mixed with a solution of 5 grams of hydroxylamine hydrochloride in as little water as possible, and then 12 grams of pure potassium hydrate dissolved in methyl alcohol slowly added. After standing for 24 hours the product was mixed with water, gently evaporated to

expel the alcohol, well cooled, and then rendered faintly acid by the addition of dilute hydrochloric acid. A considerable quantity of a white, crystalline precipitate separated, which was collected, well washed with water, dried on a porous plate, and recrystallised from light petroleum. A small quantity of oxime which remains dissolved in the aqueous liquors may be obtained as a thick oil by extracting with ether, drying over calcium chloride, and evaporating. This solidifies for the most part on standing, and may be readily purified by leaving it in contact with a porous plate till free from oily mother liquor, and then recrystallising from light petroleum. Analysis:—

0·1301 gram substance gave 0·3290 gram CO_2 and 0·1118 gram H_2O.

0·1210 gram substance gave 10·5 c.c. N; bar. = 759; $t = 14°$.

	Theory. $C_8H_{13}NO$.	Found.
C	69·06 per cent.	68·96 per cent.
H	9·36 „	9·54 „
N	10·07 „	10·31 „

Methyldihydropentenemethylketoneoxime crystallises from light petroleum in thick, colourless prisms which melt at 85°. It is readily soluble in alcohol, ether, and most other organic solvents, also in acids and alkalis.

Heated in small quantities in a test tube, it distils with only slight decomposition as a colourless oil, which on cooling solidifies completely.

Action of Beckmann's Mixture on Methyldihydropentenemethylketoneoxime.

The following experiments were instituted with the object of proving the presence of an acetyl-group in methyldihydropentene methyl ketone.

E. Beckmann, in his interesting researches on intermolecular change in oximes, has shown that methylketoneoximes under the influence of various reagents, such as phosphorus pentachloride, concentrated sulphuric acid, acetyl chloride, and especially a mixture of acetic acid and anhydride saturated with hydrogen chloride, are converted into substituted acetamides, and these when submitted to hydrolysis yield acetic acid and the corresponding primary amine, thus:—

$$R{\cdot}C(NOH){\cdot}CH_3 = RNH{\cdot}CO{\cdot}CH_3$$
$$RNH{\cdot}CO{\cdot}CH_3 + H_2O = RNH_2 + COOH{\cdot}CH_3.$$

Acetophenoneoxime under these conditions yields acetanilide, whilst methylpropylketoneoxime, $C_3H_7{\cdot}(CH_3)C{:}NOH$, is converted into

propylacetamide, $CH_3{\cdot}CO{\cdot}NH{\cdot}C_3H_7$, which then on hydrolysis yield acetic acid and aniline, or propylamine respectively. This reaction may therefore be very widely employed in determining the composition of ketones.

Methyldihydropentenemethylketoneoxime, under like treatment, might be expected to yield in the first place methyldihydropenteneacetamide :—

$$CH_3{\cdot}C(=C{\cdot}C(NOH){\cdot}CH_3)(-CH_2{\cdot}CH_2{\cdot}CH_2) = CH_3{\cdot}C(=C{\cdot}NH{\cdot}CO{\cdot}CH_3)(-CH_2{\cdot}CH_2{\cdot}CH_2).$$

which on hydrolysis would then yield methyldihydropenteneamine, and acetic acid :—

$$CH_3{\cdot}C(=C{\cdot}NH{\cdot}CO{\cdot}CH_3)(-CH_2{\cdot}CH_2{\cdot}CH_2) + H_2O = CH_3{\cdot}C(=C{\cdot}NH_2)(-CH_2{\cdot}CH_2{\cdot}CH_2) + CH_3{\cdot}COOH.$$

In order to test this, 9 grams of the oxime was dissolved in 90 grams of glacial acetic acid, 20 grams of acetic anhydride added, and the mixture saturated with hydrogen chloride, care being taken that the temperature remained below 30° during the operation. The reddish-brown solution thus obtained was heated in four sealed tubes at 100° for two hours, the resulting, bluish-black liquid transferred to a beaker, mixed with an equal bulk of water, and rendered distinctly alkaline by the addition of sodium hydrate. The dark-coloured product, which contained a quantity of a black tarry mass in suspension, was extracted ten times with ether, the ether distilled off, and the residual, dark-brown oil submitted to rapid distillation in a current of steam. The strongly alkaline distillate, containing a minute quantity of oil in suspension, was acidified with hydrochloric acid, extracted twice with ether, rendered alkaline again, saturated with anhydrous potassium carbonate, and the basic substance which was precipited as an oil extracted by agitating ten times with pure ether. The ethereal solution was dried over freshly ignited potassium carbonate, filtered, and the resulting colourless oil carefully fractioned, when the whole passed over between 160 and 170°.

After repeated fractionation over freshly ignited barium oxide, the new substance was readily obtained pure, boiling constantly at 164—165°. The analysis gave the following results :—

I. 0·1548 gram substance gave 0·3899 gram CO_2 and 0·1332 gram H_2O.

II. 0·1921 gram substance gave 0·4820 gram CO_2 and 0·1621 gram H_2O.

Ia. 0·1317 gram substance gave 12 c.c. N; bar. = 740 mm.; $t = 18$.
IIa. 0·1267 gram substance gave 10·8c.c. N; bar. = 741 mm.; $t = 18$.
III. 0·1626 gram substance gave 14·5 c.c. N; bar = 740 mm.; $t = 17$.

	Theory. $C_8H_{13}NO$.	Found. I.	II.	III.
C	69·06 p. c.	68·79	68·90	— p. c.
H	9·36 „	9·55	9·37	— „
N	10·07 „	10·45	10·05	10·25 „

This substance, $C_8H_{13}NO$, is a colourless oil possessing a very pungent and disagreeable odour, closely resembling that of pentamethylenediamine.

It mixes with water in all proportions with considerable evolution of heat, and it is also soluble in most organic solvents. With acids, it forms readily soluble salts; the platinochloride, which will be described further on, crystallises from water in magnificent, orange-red prisms.

This base is isomeric with methyldihydropentenemethylketoneoxime, and had the reaction proceeded normally, it should have the constitution—

$$\begin{matrix} CH_3\cdot C & \equiv & C\cdot NH\cdot CO\cdot CH_3 \\ | & & | \\ CH_2\cdot CH_2\cdot & & CH_2 \end{matrix}$$

From its method of purification, and especially on account of its powerful basic properties, it is very evident that this formula cannot possibly represent its constitution. Such a substance would on distillation with dilute sodium hydrate be at at once split up, yielding methyldihydropenteneamine and sodium acetate; the amides, moreover, have but very feeble basic properties; they are mostly solid substances, and boil at very high temperatures (capronamide, $C_6H_{13}NO$, boils at 255°). It is, however, extremely probable that the first step in the formation of this base is the conversion of the oxime into methyldihydropenteneacetamide—which then undergoes further intermolecular change—being converted into a stable base, containing two 5-rings; the one made up of carbon-atoms only, the other containing four carbon- and one nitrogen-atoms; thus:—

$$CH_2\!<\!\begin{matrix} CH_2\cdot C\cdot CH_3 \\ \| \\ CH_2\cdot C\cdot NH\cdot CO\cdot CH_3 \end{matrix} = CH_2\!<\!\begin{matrix} CH_2\cdot C\cdot CH_2 \\ \| \\ CH_2\cdot C\cdot NH \end{matrix}\!>\!C(OH)\cdot CH_3.$$

Platinochloride of $C_8H_{13}NO$.

This magnificent salt is readily obtained by mixing the moderately concentrated solution of the base in hydrochloric acid with an excess

of platinum chloride. The solution usually remains clear for some time, but on standing beautiful, orange-coloured tufts of crystals appear. After 24 hours these were collected, washed with water, recrystallised from this solvent, and analysed with the following results:—

I. 2081 gram substance gave 0·0788 gram H_2O, 0·2140 gram CO_2, and 0·0586 gram Pt.

Ia. 0·1479 gram substance gave 4·3 c.c. N; $t = 15°$; bar. = 750 mm.

II. 0·2957 gram substance gave 0·0839 gram Pt.

III. 0·1129 gram substance gave 0·0320 gram Pt.

	Theory. $(C_8H_{13}NO)_2H_2PtCl_6$.	Found. I.	II.	III.	
C.....	27·95 p. c.	28·04	—	—	p. c.
H.....	4·08 ,,	4·20	—	—	,,
N.....	4·08 ,,	4·32	—	—	,,
Pt.....	28·24 ,,	28·16	28·38	28·35	,,

This salt is very readily soluble in hot water, moderately soluble in cold. The strong solution in hot water, which has a deep orange-red colour, deposits the salt on cooling in magnificent, red crystals, of the following forms:—

The crystals dissolve readily in boiling absolute alcohol, forming a light-yellow solution; on cooling, the substance crystallises out in long, thin, pale-yellow needles.

When heated in a tube, the dry substance decomposes rapidly at 190—193°, turning perfectly black and giving off a quantity of gas.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, March*, 1890. Vol. LVII.]

$\omega\omega_1$-DIACETYLBUTANE.

By T. Rhymer Marshall, D.Sc., and W. H. Perkin, Jun., Ph.D.

This paper which is a continuation of the preceding one, contains a description of the preparation and properties of the following substances :—

$\omega\omega_1$-Diacetylbutane ...	$CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}CO{\cdot}CH_3$.
Methyldihydropentene-methyl ketone.....	$CH_3{\cdot}C{=}C{\cdot}CO{\cdot}CH_3$ $CH_2{\cdot}CH_2{\cdot}CH_2$
Methylpentamethylene-methyl carbinol	$CH_3{\cdot}CH{-}CH{\cdot}CH(OH){\cdot}CH_3$ $CH_2{\cdot}CH_2{\cdot}CH_2$

together with the iodide and acetate of this alcohol.

Methylethylpentamethylene.....	$CH_3{\cdot}CH{-}CH{\cdot}CH_2{\cdot}CH_3$ $CH_2{\cdot}CH_2{\cdot}CH_2$
Methylethyldihydropentene methyl ketone..	$CH_3{\cdot}C{=}C{\cdot}CO{\cdot}CH_3$ $C_2H_5{\cdot}CH{\cdot}CH_2{\cdot}CH_2$

and also of numerous other substances obtained as bye-products, in the preparation of the above compounds.

$\omega\omega_1$-*Diacetylbutane*, $CH_3{\cdot}CO[CH_2]_4{\cdot}CO{\cdot}CH_3$.

Owing to the ease with which diacetylbutane is converted into methyldihydropentene methyl ketone, it has been found extremely difficult to prepare this substance in a pure state. The following method has, however, on two or three occasions been used with success.

Five grams of pure ethyl diacetyladipate (prepared from the ammonium compound, p. 219) were dissolved in a little methyl alcohol, mixed with a slight excess of a strong solution of pure potash in methyl alcohol, and heated to boiling on a water-bath for 15 minutes. The alcoholic solution was filtered from the precipitated potassium carbonate, the filtrate mixed with twice its volume of water, neutralized with dilute sulphuric acid, and the alcohol distilled off. The residue was extracted three times with ether, the ethereal solution washed with water, dried over anhydrous potassium carbonate, and evaporated. The resulting, almost colourless oil, after standing over sulphuric acid in a vacuum for some days in a cold place, deposited a quantity of flaky crystals, and in one case solidified almost entirely.

These crystals were freed from oily impurities by spreading on a porous plate, and in this way a beautiful, colourless, flaky, crystalline mass was obtained, which on analysis gave the following numbers :—

0·1380 gram substance gave 0·1220 gram H_2O and 0·3410 gram CO_2.

	Theory. $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}CO{\cdot}CH_3$.	Found.
C	67·60 per cent.	67·39 per cent.
H	9·86 „	9·82 „
O	22·54 „	22·79 „

Diacetylbutane is a colourless, crystalline substance which, when purified as above, melts at about 43—44°. It is readily soluble in almost all organic solvents, sparingly so in water. It combines readily with hydrogen sodium sulphate, with phenylhydrazine, and with hydroxylamine, forming well characterised derivatives, which were not prepared in any quantity, or analysed owing to the difficulty experienced in obtaining sufficient pure diacetylbutane.

Under the influence of dehydrating agents, or by simply boiling with alcoholic potash, and apparently also on distillation, diacetylbutane undergoes internal condensation, yielding methyldihydropentene methyl ketone.

$$CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}CO{\cdot}CH_3 = CH_3{\cdot}C\!=\!\!=\!\!=\!C{\cdot}CO{\cdot}CH_3 \;(CH_2{\cdot}CH_2{\cdot}CH_2) + H_2O.$$

Methyldihydropentene methyl ketone, $CH_3{\cdot}C\!=\!\!=\!\!=\!C{\cdot}CO{\cdot}CH_3$ $(CH_2{\cdot}CH_2{\cdot}CH_2)$.

This substance is readily obtained by the action of strong boiling alcoholic potash on ethyl diacetyladipate. For this purpose it is not necessary to use pure ethyl diacetyladipate; the crude oil which is obtained on distilling the product of the action of ethylene bromide on ethyl sodioacetoacetate with steam, as described in the previous paper, answers equally well.

The quantities most conveniently employed are the following:—

Crude ethyl diacetyladipate, 50 grams.

Caustic potash, 50—55 grams (dissolved in the smallest quantity of boiling 80 per cent. alcohol).

The ethyl diacetyladipate is dissolved in an equal bulk of alcohol, heated to boiling on a water-bath, in a flask connected with a reflux apparatus, and one-third of the potash solution run in. After boiling vigorously for five minutes, another third of the potash solu-

tion is added, the mixture boiled for ten minutes, then the remaining potash solution added, and the alcohol at once distilled off. The dark-brown product is mixed with sufficient water to dissolve the potassium carbonate and other potash salts, extracted five times with ether, the ethereal solution washed with water, dried over anhydrous potassium carbonate, and evaporated. In this way a yellowish oil is obtained which should weigh 15 to 20 grams. On distillation, almost the whole of it passes over between 185 and 200° as a colourless oil, leaving only a very small dark residue in the retort, and on refractioning once or twice, the substance is readily obtained pure, and boiling constantly at 191° (760 mm.).

The numbers obtained on analysis agree with those required by the formula $C_8H_{12}O$.

0·1344 gram substance gave 0·1194 gram H_2O and 0·3804 gram CO_2.

	Theory. $C_8H_{12}O$.	Found.
C	77·42 per cent.	77·19 per cent.
H	9·68 „	9·87 „
O	12·90 „	12·94 „

Methyldihydropentene methyl ketone, which, by this method, may be obtained in a state of great purity with comparatively little labour, is a colourless, mobile oil, possessing a most powerful odour of peppermint.

A series of carefully conducted experiments have shown that it is identical with the compound obtained by the hydrolysis of the crude product of the distillation of ethyl diacetyladipate, as described in the foregoing paper (p. 231). Both these substances boil at the same temperature; they possess the same odour, have the same specific gravity, and give the same products on reduction.

As it was very important to be certain of the identity of the two substances, the oxime of the product obtained as above was prepared and compared with that previously obtained from the other compound, $C_8H_{12}O$ (p. 232); 1 gram of the pure substance was dissolved in methyl alcohol, mixed with a dilute methyl alcoholic solution of 0·7 gram of hydroxylamine hydrochloride and 1·5 gram of potash, and the whole allowed to stand 24 hours. The resulting, colourless solution was mixed with an equal volume of water, boiled to expel the alcohol, cooled well, and acidified with dilute sulphuric acid. The crystalline precipitate thus obtained was collected, well washed with water, dried on a porous plate, and recrystallised from light petroleum. The beautifully crystalline substance thus obtained gave the following numbers on analysis:—

I. 0·1733 gram substance gave 0·1490 gram H_2O and 0·4395 gram CO_2.

II. 0·2677 gram substance gave 23·8 c.c. N; $t = 14°$; bar. = 744.

	Theory. $C_8H_{13}NO$.	Found.
C	69·06 per cent.	69·16 per cent.
H.....	9·36 „	9·54 „
N	10·07 „	10·30 „

This oxime melts at 85°, is readily soluble in acids and alkalis, and agrees in all its properties with the substance already described in the last paper (p. 237).

As the yield of methyldihydropentene methyl ketone was far from that which should have been obtained theoretically, it was thought that interesting results might be obtained by examining the solution of the potassium salts from which the above ketone had been extracted.

The dark-brown solution was evaporated till free from alcohol, acidified with dilute sulphuric acid, and extracted several times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a dark-brown, acid-smelling oil, which, even after long standing over sulphuric acid in a vacuum, showed no signs of crystallising. In order to purify this crude product, it was dissolved in a slight excess of baryta-water, the solution heated to boiling, and treated with carbon dioxide until the excess of baryta had been removed. On filtering, the solution was found to be much less coloured, whilst the barium carbonate precipitated was distinctly brownish, showing that a considerable quantity of impurity had been removed. The boiling solution of the barium salt was acidified with dilute hydrochloric acid, well agitated, filtered from a small quantity of resinous matter, and after cooling, repeatedly extracted with ether. On drying the ethereal solution over calcium chloride and evaporating, a dark-yellow oil was obtained, which, after standing for some days over sulphuric acid in a vacuum, deposited crystals. These were separated from the oily mother liquor as completely as possible by spreading on a porous plate, and then further purified by recrystallisation from water.

The colourless crystals thus obtained gave the following results on analysis:—

I. 0·2146 gram substance gave 0·1240 gram H_2O and 0·4490 gram CO_2.

II. 0·1594 gram substance gave 0·0903 gram H_2O and 0·3323 gram CO_2.

	Theory. $CH_3\cdot C(=C\cdot COOH)\cdot CH(COOH)\cdot CH_2\cdot CH_2$	Found. I.	Found. II.
C	56·47 p. c.	56·96	56·86 p. c.
H	5·88 „	6·26	6·29 „
O	37·65 „	36·78	36·85 „

This acid melts at 188°, and is evidently identical with the substance obtained by the hydrolysis of the oil $C_{11}H_{16}O_3$, as described in the last paper. The formation of this acid by the hydrolysis of ethyl diacetyladipate would be represented by the following equation:—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CH\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 3KOH =$$

$$\begin{matrix}CH_3\cdot C=C\cdot COOK\\COOK\cdot CH\cdot CH_2\cdot CH_2\end{matrix} + CH_3\cdot COOK + H_2O + 2C_2H_5\cdot OH.$$

Action of Reducing Agents on Methyldihydropentene Methyl Ketone. Formation of Methylpentamethylene Methyl Carbinol,

$$\begin{matrix}CH_3\cdot CH & --- & CH\cdot CH(OH)\cdot CH_3\\CH_2\cdot CH_2\cdot CH_2\end{matrix}$$

The products obtained in the reduction of methyldihydropentene methyl ketone vary remarkably with the nature of the reducing agents employed; thus, whereas on treatment with sodium in ethereal solution methylpentamethylene methyl carbinol results, when sodium amalgam is employed, scarcely a trace of this substance is formed. In preparing methylpentamethylene methyl carbinol, 20 grams of the ketone was dissolved in 100 grams of ether, the solution floated on about 50 c.c. of water, and about three times the calculated quantity of sodium very gradually added, and if necessary small quantities of water, from time to time, the flask being carefully cooled by a stream of running water. As soon as all the sodium has been added, the ethereal solution was separated, washed with water, dried over potassium carbonate, evaporated, and the resulting, thick, colourless oil submitted to fractional distillation under reduced pressure (55 mm.). In this way the oil was readily separated into two principal fractions, 120—150° and 230—260°. On repeatedly refractioning the lower fraction at ordinary pressures, pure methylpentamethylene methyl carbinol was readily obtained as a colourless oil, boiling constantly at 180°.

Analyses.

I. 0·1231 gram substance gave 0·1412 gram H_2O and 0·3389 gram CO_2.

II. 0·1631 gram substance gave 0·1814 gram H_2O and 0·4487 gram CO_2.

$CH_3 \cdot CH(CH_2CH_2 \cdot CH_2) - CH \cdot CH(OH) \cdot CH_3$

	Theory.	Found. I.	Found. II.
C	75·00 p. c.	75·08	75·03 p. c.
H	12·50 „	12·74	12·35 „
O	12·50 „	12·18	12·62 „

Methylpentamethylene methyl carbinol is a colourless, moderately mobile oil, having a strong odour of menthol. It is readily soluble in organic solvents, and also slightly soluble in water.

Methylpentamethylene methyl carbinol yields an acetate when treated with acetic anhydride (p. 249), and an iodide when digested with hydriodic acid (p. 249).

In order to demonstrate the existence of a closed chain in methyl dihydropentene methyl ketone, it was important to show clearly that this substance on reduction is only capable of taking up at the most 4 atoms of hydrogen. As methylpentamethylene methyl carbinol was possibly only an intermediate product of the reduction of the ketone, experiments were made with the view of reducing this alcohol still further.

Five grams of the pure alcohol were mixed with 200 grams of absolute alcohol, heated to boiling on a water-bath, in a flask connected with a reflux apparatus, and then 20 grams of sodium thrown in as rapidly as possible. The product was mixed with water, the alcohol distilled off, and the residue extracted with ether. The resulting oil, on distillation under reduced pressure (80 mm.), distilled at 119—120°, and on subsequent fractioning under ordinary pressure at 178—181°, and gave the following numbers on analysis :—

0·1294 gram substance gave 0·1443 gram H_2O and 0·3532 gram CO_2.

	Theory. $C_8H_{16}O$.	Found.
C	75·00 per cent.	74·44 per cent.
H	12·50 „	12·39 „
O	12·50 „	13·17 „

This result tends to show that methylpentamethylene methyl carbinol is a fully saturated substance, not capable of combining further with hydrogen, a fact which is proved conclusively by the results of the experiments on the action of hydriodic acid on the iodide of this alcohol.

In reducing methyldihydropentene methyl ketone in a moist ethereal solution with sodium, a considerable quantity of a very thick oil is

obtained, which boils at about 230—260° (55 mm.). As it was thought that the examination of this substance might lead to interesting results, it was most carefully fractioned several times under a pressure of 50 mm., after which the greater part boiled at 250—255° (50 mm.).

Two separate preparations, both boiling at the same temperature, gave the following results on analysis :—

I. 0·2572 gram substance gave 0·2615 gram H_2O and 0·7230 gram CO_2.

II. 0·1568 gram substance gave 0·1574 gram H_2O and 0·4410 gram CO_2.

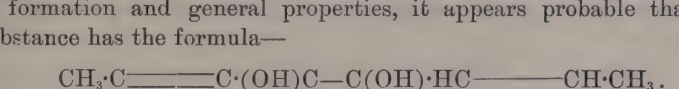
	Theory. $C_{16}H_{28}O_2$.	Found. I.	Found. II.
C	76·19 p. c.	76·88	76·65 p. c.
H	11·11 „	11·29	11·15 „
O	12·70 „	11·83	12·20 „

A determination of its molecular weight by Raoult's method, using acetic acid as a solvent, gave the following results :—

Weight of substance	1·2890
„ acetic acid.....	50·17
Melting point of acetic acid	15·74°
„ mixture.....	15·33
Depression of m. p.....	0·41

Molecular weight, $C_{16}H_{28}O_2$, 252. Found, 244.

This substance, which appears to have the formula $C_{16}H_{28}O_2$, is a colourless, transparent syrup, so thick that a test-tube half full of the syrup may be inverted for some time without the substance falling out. It has a decided odour of menthol, distils at the ordinary pressure with slight decomposition, and under reduced pressure (50 mm.) at 250—255°, without the slightest decomposition. From its mode of formation and general properties, it appears probable that this substance has the formula—



being a condensation-product derived from 1 mol. of ethyldihydropentene methyl ketone, and 1 mol. of methylpentamethylene methyl ketone.

Reduction of Methyldihydropentene Methyl Ketone by Sodium Amalgam.

During the first experiments on the reduction of this ketone, several attempts were made to obtain the unsaturated alcohol $CH_3\cdot C\overset{CH_2\cdot CH_2\cdot CH_2}{=\!=\!=\!=} C\cdot CH(OH)\cdot CH_3$ by the action of sodium amalgam on dilute alcoholic solutions of the substance.

The pure ketone was dissolved in 50 per cent. alcohol, and treated with a large excess of 1½ per cent. sodium amalgam, the oil which soon separates out being kept in solution by the addition of further quantities of alcohol. The product of the reaction was a very thick oil, which on fractioning under a pressure of 25 mm. separated into two principal fractions, 220—225° and 250—260°, scarcely a trace of any low boiling substance being obtained.

Fraction 250—260° (25 mm.), which was a very thick, slightly brownish oil, gave on analysis the following numbers :—

0·1800 gram substance gave 0·1703 gram H_2O and 0·5086 gram CO_2.

	Theory $C_{16}H_{26}O_2$.	Found.
C	76·80 per cent.	77·05 per cent.
H	10·40 „	10·51 „
O	12·80 „	12·44 „

A determination of its molecular weight by Raoult's method gave the following results :—

Weight of substance.....	1·2797 gram.
„ acetic acid	49·14 „
Melting point of acetic acid.....	15·76°
„ mixture.....	15·34°
Depression of melting point.....	0·42°

Molecular weight of $C_{16}H_{26}O_2$, 250. Found, 242.

This substance is evidently the pinacone of methyldihydropentene methyl ketone, and its constitution must therefore be represented by the formula—

$$CH_3\cdot C\overset{CH_2\cdot CH_2\cdot CH_2}{=\!=\!=\!=} C\cdot(OH)C\overset{H_3C}{-}\overset{CH_3}{C}(OH)\cdot C\overset{CH_2\cdot CH_2\cdot CH_2}{=\!=\!=\!=} C\cdot CH_3 .$$

The fraction 220—225° (25 mm.) obtained in the reduction of methyldihydropentene methyl ketone with sodium amalgam gave on analysis numbers agreeing approximately with the formula $C_{16}H_{24}O$ (*i.e.*, $C_{16}H_{26}O_2 - H_2O$), and it is, therefore, probably an anhydride of the above pinacone. As we had only a very small quantity of this

substance at our disposal, no further experiments were made with it. It is a very thick, slightly brownish oil, having a faint odour of peppermint.

Methylpentamethylene Methyl Carbinyl Acetate,

$$CH_3\cdot CH\begin{array}{l}\text{———}\\ CH_2\cdot CH_2\cdot CH_2\end{array}CH\cdot CH(C_2H_3O_2)\cdot CH_3$$

In preparing this substance, the pure alcohol was boiled with twice the calculated quantity of acetic anhydride on a reflux apparatus for two hours, the acetic acid and excess of anhydride distilled off, and the residual oil distilled under reduced pressure.

The fraction boiling at 145—150° (130 mm.), gave on analysis the following numbers:—

0·1531 gram substance gave 0·1459 gram H_2O and 0·3960 gram CO_2.

	Theory. $C_{10}H_{18}O_2$.	Found.
C	70·58 per cent.	70·54 per cent.
H	10·60 „	10·59 „
O	18·82 „	18·87 „

This acetate is an agreeably smelling and strongly refracting liquid, which appears to distil under the ordinary pressure without decomposition. In order to more clearly prove its constitution, it was hydrolysed by boiling with excess of standard potash solution for six hours, and the amount of acetate formed determined by estimating the amount of unused alkali present in the solution by means of standard sulphuric acid. It was thus found that 1·349 gram substance on hydrolysis neutralised 79·5 c.c. of standard potash solution, 1 c.c. of which was equal to 0·00597 gram of $CH_3\cdot COOH$. This corresponds to 35·1 per cent. of $CH_3\cdot COOH$, whereas theory requires 35·3 per cent.

Methylpentamethylene Methyl Carbinyl Iodide (Methyl-α-iodethylpentamethylene 1.2),

$$CH_3\cdot CH\begin{array}{l}\text{———}\\ CH_2\cdot CH_2\cdot CH_2\end{array}CH\cdot CHI\cdot CH_3$$

Methylpentamethylene methyl carbinol is readily attacked by boiling hydrochloric, hydrobromic, and hydriodic acids, with formation of heavy oils, consisting no doubt of the corresponding chloride, bromide, and iodide of the alcohol. Of these the latter only has been prepared in quantity and examined. It is best obtained by boiling the alcohol with an excess of hydriodic acid of sp. gr. 1·96 for about half an hour on a reflux apparatus. The product is mixed with twice

its volume of water, extracted several times with ether, the ethereal solution washed well with water and dilute sodium carbonate solution, dried over anhydrous potassium carbonate, and evaporated, the resulting oil, after removing free iodine by shaking with mercury, being purified by fractionation under reduced pressure (90 mm.). A considerable portion of the substance distilled between 155 and 160° (90 mm.), and gave on analysis the following numbers:—

0·2543 gram substance heated with nitric acid and nitrate of silver at 180° for four hours gave 0·2460 gram AgI.

	Theory. $C_8H_{15}I$.	Found.
I	53·21 per cent.	52·26 per cent.

This iodide is a colourless, heavy oil, having an odour strongly resembling that of hexyl iodide. When distilled, even under reduced pressure, it undergoes slight decomposition, with formation of products of high boiling point; it is better for most purposes, therefore, to use the crude oil, without fractioning.

Methylethylpentamethylene (1.2), $\begin{matrix} CH_3\cdot CH & \text{———} & CH\cdot CH_2\cdot CH_3 \\ | & & | \\ CH_2\cdot CH_2\cdot CH_2 & & \end{matrix}$.

In preparing this interesting substance, methyl-α-iodethylpentamethylene was heated in sealed tubes with excess of the strongest hydriodic acid and a little amorphous phosphorus at 240—250° for 12 hours. The contents of several tubes, each of which had contained about 5 grams of the iodide, were transferred to a separating funnel, allowed to stand for some hours, and the dark-coloured aqueous liquid separated as completely as possible from the layer of hydrocarbon which floated on the surface. The residual, limpid oil, after drying over potassium carbonate and distilling, passed over completely between 120 and 130°, and after repeated distillation over sodium and lastly over potassium the pure substance was obtained boiling constantly at 124°. The analysis gave the following numbers:—

I. 0·1313 gram substance gave 0·1708 gram H_2O and 0·4136 gram CO_2.

II. 0·1100 gram substance gave 0·1435 gram H_2O and 0·3465 gram CO_2.

	Theory. C_8H_{16}.	Found. I.	Found. II.
C	85·71 p. c.	85·91	85·71 p. c.
H	14·29 „	14·45	14·30 „

A determination of the vapour-density of this substance, by Victor Meyer's method, in aniline vapour gave the following results:—

0·042 gram substance displaced 8·5 c.c. of air; $t = 13°$ C.; bar. = 755 mm.

Molecular weight calculated, 118. Found, 112.

Methylethylpentamethylene is only with difficulty attacked by bromine; on boiling the two substances together, slight action takes place with evolution of hydrogen bromide. On shaking the hydrocarbon with fuming hydrobromic acid (sp. gr. 1·85) even for days, no appreciable action could be detected. When boiled with nitric acid (sp. gr. 1·16), oxidation rapidly sets in, and in the course of a few hours the oily layer of hydrocarbon entirely disappears and a colourless solution is obtained from which no definite substance could be extracted.

Ethylmethyldihydropentene Methyl Ketone, $\begin{matrix} CH_3\cdot C \!=\!\!=\!\!= C\cdot CO\cdot CH_3 \\ C_2H_5\cdot CH\cdot CH_2\cdot CH_2 \end{matrix}$.

In order to get some further proof of the constitution of methyldihydropentene methyl ketone, several experiments were made with the object of preparing diethyldiacetylbutane,

$$CH_3\cdot CO\cdot CH(C_2H_5)\cdot CH_2\cdot CH_2\cdot CH(C_2H_5)\cdot CO\cdot CH_3,$$

and studying its behaviour towards dehydrating agents.

A short time since, Dr. Kipping and one of us (this vol., p. 29 *et seq.*) prepared diethyldiacetylpentane by treating ethylic ethylacetoacetate with sodium ethylate and trimethylene bromide, and hydrolysing the resulting ethylic diethyldiacetylpimelate, thus:—

$$2\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!>\!CNa\cdot C_2H_5 + C_3H_6Br_2 =$$

$$\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!>\!C(C_2H_5)\cdot[CH_2]_3\cdot C(C_2H_5)\!<\!\begin{matrix} CO\cdot CH_3 \\ COOC_2H_5 \end{matrix} + 2NaBr.$$

Ethyl diethyldiacetylpimelate.

$$\begin{matrix} CH_3\cdot CO \\ COOC_2H_5 \end{matrix}\!>\!C(C_2H_5)\cdot[CH_2]_3\cdot C(C_2H_5)\!<\!\begin{matrix} CO\cdot CH_3 \\ COOC_2H_5 \end{matrix} + 4KOH =$$

$$CH_3\cdot CO\cdot CH(C_2H_5)\cdot[CH_2]_3\cdot CH(C_2H_5)\cdot CO\cdot CH_3 + 2K_2CO_3 + 2C_2H_5\cdot OH.$$

Diethyldiacetylpentane.

In endeavouring to prepare diethyldiacetylbutane by substituting ethylene bromide for trimethylene bromide in the above equation, we obtained only a trace of substance of high boiling, which might have been diethyl diacetyladipate, the principal product of the reaction being ethyl butyrate.

We then experimented on the action of ethyl iodide on the disodium compound of ethyl diacetyladipate in the hope of thus obtaining ethylic diethyldiacetyladipate, according to the equation

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!CNa\cdot CH_2\cdot CH_2\cdot CNa\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 2C_2H_5I =$$

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!C(C_2H_5)\cdot CH_2\cdot CH_2\cdot C(C_2H_5)\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 2NaI.$$

A mixture of 60 grams of crude ethyl diacetyladipate and 60 grams of ethyl iodide were slowly added, with careful cooling, to a solution of sodium ethylate, prepared by dissolving 9·7 grams of sodium in 100 grams of absolute alcohol. The whole was transferred to a soda-water bottle and heated on a water-bath for 12 hours. The alcohol was then distilled off, sufficient water added to dissolve the inorganic salts, and the product extracted four times with ether. The ethereal solution was washed with water, the ether distilled off, and the residual oil at once hydrolysed by boiling with alcoholic potash, the same quantities and the same method of procedure being employed as in the case of ethyl diacetyladipate itself. As soon as hydrolysis was complete the alcohol was distilled off, water added, and the oil which separated repeatedly extracted with ether. The ethereal solution, after washing with water, drying over anhydrous potassium carbonate, and evaporating, deposited a considerable quantity of a brownish oil which, on distillation, all passed over between 200° and 270°. This, on repeated fractionation, separated into two fractions, 210—215° and 250—255°, the latter, however, being very small.

Fraction 210—215° gave the following results on analysis:—

0·1199 gram of substance gave 0·1149 gram H_2O and 0·3375 gram CO_2.

	Theory. $C_{10}H_{16}O$.	Found.
C	78·94 per cent.	78·74 per cent.
H	10·53 „	10·57 „
O	10·53 „	10·69 „

This substance is evidently ethylmethydihydropentene methyl ketone, formed from ethylic ethyldiacetyladipate according to the equation—

$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!\!>\!C(C_2H_5)\cdot CH_2\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 4KOH =$$

$$\begin{matrix}CH_3\cdot C\!=\!\!=\!\!=\!C\cdot CO\cdot CH_3\\C_2H_5\cdot CH\cdot CH_2\cdot CH_2\end{matrix} + 2K_2CO_3 + 2C_2H_5\cdot OH + H_2O.$$

In order to corroborate this, the substance was converted into its oxime. 4 grams of the oil were dissolved in a little methyl alcohol, and mixed with 4 grams of hydroxylamine hydrochloride dissolved in a small quantity of water, and 10 grams of pure potash dissolved in methyl alcohol. After 24 hours, the alcohol was evaporated by gently warming the solution on a water-bath, the residue mixed with water, rendered faintly acid by the addition of a few drops of hydrochloric acid, and repeatedly extracted with pure ether. The ethereal solution, after well washing with water, drying over calcium chloride, and evaporating, deposited the oxime as an oil which showed no signs of crystallisation on standing for 24 hours over sulphuric acid in a vacuum. The analysis gave the following numbers:—

0·1286 gram substance gave 9·4 c.c. N; bar. = 740 m.; $t = 13°$.

	Theory. $C_{10}H_{17}NO$.	Found.
N	8·38 per cent.	8·40 per cent.

The fraction 250—255° appeared to consist of impure diethyldiacetylbutane, but the quantity obtained was so small that it was found impossible to obtain it in a pure state. With hydroxylamine it gave a solid dioxime.

We hope to be able to prepare this interesting substance by some other reaction, and to study its behaviour with dehydrating agents with a view of proving the formula given in this and the previous paper for methyldihydropentene methyl ketone.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE

THE SYNTHETICAL FORMATION OF CLOSED CARBON CHAINS. Part I (*continued*). THE ACTION OF ETHYLENE BROMIDE ON THE SODIUM COMPOUNDS OF ETHYL ACETOACETATE AND ETHYL BENZOYLACETATE.

By T. Rhymer Marshall, D.Sc., and W. H. Perkin, Jun., Ph.D., F.R.S.

In the study of the synthetical formation of closed carbon chains, one of the most difficult problems has been the determination of the constitution of those substances which are produced when ethylene bromide reacts with the sodium compounds of ethyl malonate, ethyl acetoacetate, and ethyl benzoylacetate.

Taking in the first place the product of the action of ethylene bromide on the sodium compound of ethyl malonate, this substance may be represented either as ethyl trimethylenedicarboxylate (Perkin, Trans., 1885, **47**, 807; 1887, **51**, 849; *Ber.*, **17**, 54), or as ethyl vinylmalonate (Fittig, Roeder, *Ber.*, **16**, 372):

I. $(COOC_2H_5)_2CNa_2 + C_2H_4Br_2 = (COOC_2H_5)_2C<\begin{matrix}CH_2\\|\\CH_2\end{matrix} + 2NaBr.$

II. $(COOC_2H_5)_2CNa_2 + C_2H_4Br_2 = (COOC_2H_5)_2CH\cdot CH{:}CH_2 + 2NaBr.$

The difficulty in distinguishing between these formulæ lies in the fact that the acid obtained from this ethereal salt by hydrolysis behaves in some respects as an unsaturated acid, whereas in other respects its reactions point to its being a saturated substance. The careful study of the chemical properties and the magnetic rotation of the ethereal salt has, however, left scarcely any doubt that this substance is, in reality, ethyl trimethylenedicarboxylate, and this view of its constitution has received additional support from the very interesting work of Buchner on trimethylene derivatives (*Synthesen von Pyrazol-, Pyrazolin- und Trimethylen-derivaten mittels Diazoessigäther: Habilitationsschrift*, München, 1891).

Baeyer's permanganate test, which of late has come so much into prominence, has been applied by Buchner as a means of discriminating between trimethylene derivatives and unsaturated substances.

This test is based on the fact, first observed by Baeyer (*Annalen*, **245**, 146), that dilute alkaline solutions of unsaturated acids decolorise potassium permanganate instantly, whereas in the case of saturated acids, the pink colour often remains unchanged for days.

Büchner thus found that trimethylenedicarboxylic acid, and in fact all the trimethylenecarboxylic acids as yet described, behave as saturated substances, and therefore cannot be vinyl derivatives.

Turning now to the product of the action of ethylene bromide on the sodium derivative of ethyl acetoacetate, the problem of assigning the correct constitution to this substance is found to be much more difficult.

The reaction in question undoubtedly proceeds as follows:—

$$2CH_3{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_2H_4Br_2 = C_8H_{12}O_3 + CH_3{\cdot}CO{\cdot}CH_2{\cdot}COOC_2H_5 + 2NaBr.$$

There are four formulæ which may be devised to represent the constitution of this ethereal salt $C_8H_{12}O_3$, namely:—

I. $\begin{matrix}COOC_2H_5\\CH_3{\cdot}CO\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH_2\\|\\CH_2{\cdot}\end{matrix}$ *Ethyl acetyltrimethylenecarboxylate.*

II. $\begin{matrix}COOC_2H_5\\CH_3{\cdot}CO\end{matrix}\!\!>\!CH{\cdot}CH{:}CH_2.$ *Ethyl vinylacetoacetate.*

III. $\begin{matrix}COOC_2H_5{\cdot}C{:}C(CH_3)\\|\\CH_2{\cdot}CH_2\end{matrix}\!\!>\!O.$ *Ethyl methyldehydropentonecarboxylate.*

IV. $\begin{matrix}COOC_2H_5{\cdot}CH{\cdot}C(:CH_2)\\|\\CH_2\text{——}CH_2\end{matrix}\!\!>\!O.$ *Ethyl methylenetetrahydrofurfurancarboxylate.*

The formation of the compounds represented in I and II corresponds with the formation of ethyl trimethylenedicarboxylate and ethyl vinylmalonate respectively, as represented by the equations at the commencement of this paper.

Ethyl methyldehydropentonecarboxylate (III) would be produced as follows:—

$$CH_3{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_2H_4Br_2 = CH_3{\cdot}CO{\cdot}CH(CH_2{\cdot}CH_2Br){\cdot}COOC_2H_5 + NaBr.$$

Ethyl ω-bromethylacetoacetate.

This intermediate product, under the influence of a second molecule of ethyl sodacetoacetate, loses 1 mol. of hydrogen bromide, thus:—

$$CH_3{\cdot}CO{\cdot}CH(CH_2{\cdot}CH_2Br){\cdot}COOC_2H_5 = CH_3{\cdot}C(OH){:}C(CH_2{\cdot}CH_2Br){\cdot}COOC_2H_5 =$$

Labile form.

$$\begin{matrix}COOC_2H_5{\cdot}C{:}C(CH_3)\\|\\CH_2{\cdot}CH_2\end{matrix}\!\!>\!O + HBr,$$

a reaction which is similar to that which has been proved to take place between ethyl sodacetoacetate and trimethylene bromide (Trans., 1887, **51**, 702—727; Lipp, *Ber.*, **18**, 3277).

Ethyl methylenetetrahydrofurfurancarboxylate (IV) may be supposed to be produced from ethyl ω-bromethylacetoacetate in the following way:—

$$CH_3\cdot CO\cdot CH(CH_2\cdot CH_2Br)\cdot COOC_2H_5 =$$
$$CH_2{:}C(OH)\cdot CH(CH_2\cdot CH_2Br)\cdot COOC_2H_5 =$$
Labile form.
$$COOC_2H_5\cdot CH\cdot C(:CH_2)$$
$$CH_2 - CH_2 > O + HBr.$$

In previous investigations (Perkin, Trans., 1885, **47**, 801; Freer and Perkin, Trans., 1887, **51**, 820), experiments on the behaviour of the ethereal salt $C_8H_{12}O_3$, and the corresponding acid $C_6H_8O_3$, under the influence of various reagents, were described, and the results thus obtained were shown to lead to the conclusion that this ethereal salt consisted for the most part of ethyl acetyltrimethylenecarboxylate mixed with varying, but usually very small, quantities of ethyl methyldehydropentonecarboxylate.

Subsequently Lipp (*Ber.*, **22**, 1210; compare Colman and Perkin, Trans., 1889, **55**, 358) repeated these experiments, and came to the conclusion that this ethereal salt was ethyl methylenetetrahydrofurfurancarboxylate,* and could not possibly be ethyl acetyltrimethylenecarboxylate.

Owing to these conflicting opinions, it appeared to us that it would be interesting to still further investigate the subject, and in doing so we have obtained a number of results, which, as we believe, conclusively prove that this ethereal salt $C_8H_{12}O_3$ is (as was already suggested by Freer and Perkin) a mixture of ethyl acetyltrimethylenecarboxylate and ethyl methyldehydropentonecarboxylate, the former as a rule largely predominating.

In discussing the question of the constitution of these substances, it will perhaps be best to take each of the possible formulæ separately, and then, by submitting it to the test of experimental evidence, to endeavour to discriminate between them.

As already stated, the ethereal salt $C_8H_{12}O_3$ undoubtedly contains traces of a second substance, but, for the sake of simplicity, the pre-

* Lipp names the substance $\begin{matrix}COOC_2H_5\cdot CH\cdot C(:CH_2)\\ CH_2 - CH_2\end{matrix}>O$ "ethyl trihydromethylenefurfurancarboxylate;" but an examination of the formula reveals at once the fact that this substance is a derivative of tetrahydrofurfuran, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>O$, *i.e.*, ethyl methylenetetrahydrofurfurancarboxylate.

sence of this substance may in the meantime be left out of consideration without in the least affecting the question of the constitution of the ethereal salt itself.

Firstly, then, this ethereal salt $C_8H_{12}O_3$ cannot be *ethyl vinylacetoacetate*, $CH_3{\cdot}CO{\cdot}CH(CH{:}CH_2){\cdot}COOC_2H_5$, because—

1. On hydrolysis, it yields the corresponding acid, $C_6H_8O_3$, without decomposition (Trans., 1885, **47**, 831). Ethyl vinylacetoacetate would, under similar conditions, act presumably like all other monosubstituted derivatives of ethyl acetoacetate, and be completely decomposed into vinylacetone and acetic and vinylacetic acids:—

$$2CH_3{\cdot}CO{\cdot}CH(CH{:}CH_2){\cdot}COOC_2H_5 + 4KOH = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH{:}CH_2 + CH_2{:}CH{\cdot}CH_2{\cdot}COOK + CH_3{\cdot}COOK + K_2CO_3 + 2C_2H_5{\cdot}OH.$$

(Compare hydrolysis of ethyl allylacetoacetate.)

2. Ethyl vinylacetoacetate, being a monosubstituted derivative of ethyl acetoacetate, should, when treated with sodium ethylate and an alkyl iodide such as isoamyl iodide, yield a higher homologue, *e.g.*, ethyl isoamylvinylacetoacetate, thus:—

$$CH_3{\cdot}CO{\cdot}CNa(CH{:}CH_2){\cdot}COOC_2H_5 + C_5H_{11}I = CH_3{\cdot}CO{\cdot}C(C_5H_{11})(CH{:}CH_2){\cdot}COOC_2H_5 + NaI.$$

Similarly, ethyl ethylacetoacetate, when treated with sodium ethylate and ethylene bromide, should yield ethyl ethylvinylacetoacetate, which should possess properties similar to those of the ethereal salt $C_8H_{12}O_3$:—

$$2CH_3{\cdot}CO{\cdot}CNa(C_2H_5){\cdot}COOC_2H_5 + C_2H_4Br_2 = CH_3{\cdot}CO{\cdot}C(C_2H_5)(CH{:}CH_2){\cdot}COOC_2H_5 + CH_3{\cdot}CO{\cdot}CH(C_2H_5){\cdot}COOC_2H_5 + 2NaBr.$$

Neither of these reactions was found to take place on instituting the experiments.

3. Baeyer's permanganate test shows the acid $C_6H_8O_3$ to be a saturated acid, whereas vinylacetoacetic acid is unsaturated.

4. The magnetic rotation of the pure ethereal salt $C_8H_{12}O_3$ is 8·198, whereas the magnetic rotation of ethyl vinylacetoacetate (calculated from that of ethyl allylacetoacetate) would be 9·360 (Trans., 1887, **51**, 822, 823, 828).

Secondly. The substance $C_8H_{12}O_3$ cannot be the ethereal salt of methyldehydropentonecarboxylic acid, because this acid has been prepared by us, and differs very widely from the acid $C_6H_8O_3$ obtained by the hydrolysis of the ethereal salt $C_8H_{12}O_3$, as is seen from the following table:—

Acid $C_6H_8O_3$.	*Methyldehydropentonecarboxylic Acid.*
Oil.	White crystals, m. p. 150°.
Miscible with water.	Only moderately soluble in water.
Gives with hydroxylamine an oxime, $C_6H_9NO_3$.	Is not acted on by hydroxylamine.
On distillation yields acetyltrimethylene, b. p. 112°, which is not acted on by water.	On distillation yields methyldehydropentone, b. p. 82°, which, in contact with water is converted into acetopropyl alcohol.
Is not oxidised by potassium permanganate in dilute alkaline solution.	The dilute alkaline solution of this acid reduces potassium permanganate instantly.

That the acid described above as methyldehydropentonecarboxylic acid has the constitution represented by the formula

$$\begin{matrix} COOH\cdot C{:}C(CH_3) \\ \quad\quad | \quad\quad > O \\ \quad CH_2\cdot CH_2 \end{matrix}$$

is rendered extremely probable by the following considerations:—

This acid, on distillation, yields methyldehydropentone and carbon dioxide. Methyldehydropentone dissolves in water, and is converted into acetopropyl alcohol; it is therefore the anhydride of acetopropyl alcohol, and the acid must be the carboxylic acid of the anhydride of acetopropyl alcohol.

In forming an internal anhydride, acetopropyl alcohol can lose the elements of water in two ways:—

I. $CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH = \underset{\text{Labile form.}}{CH_3\cdot C(OH){:}CH\cdot CH_2\cdot CH_2\cdot OH} =$

$$\begin{matrix} CH_3\cdot C{:}CH\cdot CH_2 \\ \quad O\text{——}CH_2 \end{matrix} + H_2O.$$

II. $CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH = \underset{\text{Labile form.}}{CH_2{:}C(OH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH} =$

$$\begin{matrix} CH_2{:}C\cdot CH_2\cdot CH_2 \\ \quad O\text{——}CH_2 \end{matrix} + H_2O.$$

Apart from the improbable nature of the process, which, as far as we know, is without analogy, the reaction II, involving the participation of the methyl group in the anhydride formation, is unlikely for several reasons, especially as a similar internal anhydride is formed from benzoylpropyl alcohol, $C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$ (Trans., 1887, **57**, 838).

In this communication we shall therefore assume that the formula given above to methyldehydropentonecarboxylic acid is correct.

Thirdly. The substance $C_8H_{12}O_3$ cannot be the ethereal salt of methylenetetrahydrofurfurancarboxylic acid, because :—

1. All furfurancarboxylic acids hitherto investigated in cold dilute alkaline solution instantly decolorise potassium permanganate solution (Baeyer, *Annalen*, **256**, 193), whereas the acid $C_6H_8O_3$ is not oxidised by permanganate under these conditions.

2. The acid $C_6H_8O_3$ is a ketonic acid, because when treated with hydroxylamine it yields an oxime, $C_6H_9NO_3$.

3. The acid $C_6H_8O_3$, on reduction, takes up in the first place 2 atoms of hydrogen, yielding an acid of the formula $C_6H_{10}O_3$, which, on further reduction, is converted into α-ethyl-β-hydroxybutyric acid, $CH_3{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH$.

This reaction, it appears to us, cannot be explained in any simple manner on the assumption that the acid $C_6H_8O_3$ is methylenetetrahydrofurfurancarboxylic acid.

Similarly, the substance C_5H_8O, which is produced from the acid $C_6H_8O_3$ by the elimination of carbon dioxide, is a ketone yielding an oxime, C_5H_9NO; this ketone, on reduction, is converted into methylpropylcarbinol. These two facts show that it cannot be methylenedihydrofurfuran, $\begin{matrix}CH_2{\cdot}C(:CH_2)\\ |\\ CH_2\text{——}CH_2\end{matrix}\!>\!O$.

Fourthly. The following considerations prove, as it appears to us, that the acid $C_6H_8O_3$ is acetyltrimethylenecarboxylic acid,

$$\begin{matrix}CH_3{\cdot}CO\\ COOH\end{matrix}\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix},$$

and that the original ethereal salt $C_8H_{12}O_3$ is therefore ethyl acetyltrimethylenecarboxylate.

1. It is a monobasic ketonic acid, and as such yields an oxime, $C_6H_9NO_3$. On reduction it is converted into hydroxyethyltrimethylenecarboxylic acid, $\begin{matrix}COOH\\ CH_3{\cdot}CH(OH)\end{matrix}\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}$.

2. It is a saturated acid, as is shown by Baeyer's permanganate test.

3. On distillation, it is converted into acetyltrimethylene with elimination of carbon dioxide:

$$\begin{matrix}CH_3{\cdot}CO\\ COOH\end{matrix}\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} = CH_3{\cdot}CO{\cdot}CH\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + CO_2.$$

Acetyltrimethylene is a ketone; it dissolves readily in sodium hydrogen sulphite solution, and when treated with hydroxylamine yields a beautifully crystalline oxime, C_5H_9NO.

4. It is also interesting to note that the above-mentioned substances

show some remarkable reactions which are analogous to those first noticed in the case of trimethylene and trimethylenedicarboxylic acid.

Thus acetyltrimethylene, in contact with fuming hydrobromic acid, is converted quantitatively into acetopropyl bromide:

$$CH_3{\cdot}CO{\cdot}CH\begin{<}{CH_2\atop CH_2}\end{} + HBr = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br.$$

When heated with dilute hydrochloric acid at 100°, acetyltrimethylene is hydrolysed with formation of acetopropyl alcohol:

$$CH_3{\cdot}CO{\cdot}CH\begin{<}{CH_2\atop CH_2}\end{} + H_2O = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

Ethyl acetyltrimethylenecarboxylate dissolves readily in fuming hydrobromic acid with formation of ethyl ω-bromethylacetoacetate:

$$\begin{matrix}COOC_2H_5\\CH_3{\cdot}CO\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}CH_2\\CH_2\end{matrix} + HBr = \begin{matrix}COOC_2H_5\\CH_3{\cdot}CO\end{matrix}\!\!>\!CH{\cdot}CH_2{\cdot}CH_2Br.$$

Acetyltrimethylenecarboxylic acid, on prolonged boiling with water, is converted into acetopropyl alcohol, with elimination of carbon dioxide:

$$\begin{matrix}CH_3{\cdot}CO\\COOH\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}CH_2\\CH_2\end{matrix} + H_2O = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH{\cdot}OH + CO_2.$$

Reactions similar to the above have been noticed in the case of trimethylenedicarboxylic acid. Fittig and Roeder (*Ber.*, **16**, 2592) have shown that this acid in contact with hydrobromic acid yields ω-bromethylmalonic acid, and that when digested with dilute sulphuric acid, it is converted into butyrolactone with evolution of carbon dioxide:—

$$\begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!C(COOH)_2 + HBr = CH_2Br{\cdot}CH_2{\cdot}CH(COOH)_2.$$

$$\begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!C(COOH)_2 + H_2O = OH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH + CO_2.$$

$$OH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH = \begin{matrix}CH_2{\cdot}CH_2{\cdot}CH_2\\O\text{———}CO\end{matrix} + OH_2.$$

Again, trimethylene itself is readily acted on by hydrobromic acid, yielding propyl bromide:

$$\begin{matrix}CH_2\\CH_2\end{matrix}\!\!>\!CH_2 + HBr = CH_3{\cdot}CH_2{\cdot}CH_2Br,$$

and Gustavson (*J. pr. Chem.* [2], **36**, 300) has lately made the interesting observation that trimethylene in contact with sulphuric acid is converted into propyl alcohol:

$$\begin{matrix}CH_2\\|\\CH_2\end{matrix}\!>\!CH_2 + H_2O = CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

It will thus be seen that acetyltrimethylenecarboxylic acid and acetyltrimethylene show the reactions of trimethylene derivatives.

Lipp (*Ber.*, **22**, 1210) objects to these substances being represented as trimethylene derivatives, principally on the ground that acetopropyl bromide, when treated with solid potassium hydrate, yields a substance boiling at 110—111° which is isomeric with methyldehydropentone, and which he suggests is identical with our acetyltrimethylene. This decomposition he formulates thus:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br = CH_2{:}C(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br = \begin{matrix}CH_2{:}C{\cdot}CH_2{\cdot}CH_2\\|\qquad\qquad|\\O\!-\!-\!-\!-CH_2\end{matrix} + HBr.$$

This substance (methylenetetrahydrofurfuran) combines with phenylhydrazine, and Lipp therefore at once concludes that this property can no longer be accepted as final in distinguishing ketones from furfuran derivatives, and that, moreover, the experiment proves that the whole series of substances described by us as trimethylene derivatives are in reality tetrahydrofurfuran derivatives.

But Lipp has overlooked the fact that the decomposition of acetopropyl bromide by potassium hydrate may also be represented by either of the following equations:—

$$\text{I.}\quad CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH{:}CH_2 + HBr,$$

$$\text{II.}\quad CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br = CH_3{\cdot}CO{\cdot}CH\!<\!\begin{matrix}CH_2\\|\\CH_2\end{matrix} + HBr,$$

and, as a result of our experiments, there can be no doubt that Lipp's substance is, in reality, acetyltrimethylene, and this being a ketone naturally combines with phenylhydrazine.

Moreover, it is shown in the body of this paper that methyldehydropentonecarboxylic acid, $\begin{matrix}COOH{\cdot}C{:}C(CH_3)\\|\qquad\qquad\\CH_2{\cdot}\,CH_2\end{matrix}\!>\!O$, although its constitution is similar to that of Lipp's hypothetical methylenetetrahydrofurfuran, does not combine with hydroxylamine or phenylhydrazine at the ordinary temperature; and thus the value of phenylhydrazine as a reagent is not affected by Lipp's experiments.

At the conclusion of his paper (*loc. cit.*, p. 1211), Lipp states that dihydromethylenefurfuran (methyldehydropentone) and trihydro-

methylenefurfuran (acetyltrimethylene) combine with phenylhydrazine, yielding the same substance as is obtained by the action of phenylhydrazine on acetopropyl alcohol. Lipp describes this latter substance (*loc. cit.*, p. 1203), the formation of which he explains by the equation

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH + C_6H_5{\cdot}NH{\cdot}NH_2 = \begin{matrix} CH_3{\cdot}C{\cdot}CH_2{\cdot}CH_2 \\ \| \quad\quad\quad\quad \\ N{\cdot}N(C_6H_5) \end{matrix}\!\!>\!CH_2 + 2H_2O,$$

as a reddish-brown oil, which, on exposure to the air, becomes dark reddish-brown, and ultimately resinifies; and he gives absolutely no proof that this uninviting product is identical with the similar reddish-brown oils which he obtained from methyldehydropentone and acetyltrimethylene by the action of phenylhydrazine. As from the nature of these substances it appeared to us that it would be scarcely possible, either directly or indirectly, to prove or disprove Lipp's statement, we carried out the analogous experiment with hydroxylamine instead of with phenylhydrazine.

Acetopropyl alcohol combines readily with hydroxylamine yielding an oxime, $CH_3{\cdot}C(:NOH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$; this oxime, when heated at 100°, is converted into its anhydride, thus :—

$$CH_3{\cdot}C(NOH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH = \begin{matrix} CH_3{\cdot}C{\cdot}CH_2{\cdot}CH_2 \\ \| \quad\quad\quad\quad \\ N{-}O{-}CH_2 \end{matrix} + H_2O.$$

Now, this substance should, according to Lipp's argument, be identical with the oxime of acetyltrimethylene, if this latter compound is, as Lipp supposes, an anhydride of acetopropyl alcohol (methylenetetrahydrofurfuran), but as a fact the two differ entirely in their properties; the former is an oil, the latter a beautifully crystalline substance.

In carrying out this investigation of the acetyltrimethylene derivatives, we have also included a further study of the benzoyltrimethylene derivatives (Trans., 1885, **47**, 836—849; 1887, **51**, 837), in order to obtain further evidence to prove that these two series of compounds are analogously constituted.

It will be remembered that ethyl benzoyltrimethylenecarboxylate is produced by the action of sodium ethylate and ethylene bromide on ethyl benzoylacetate :—

$$C_6H_5{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_2H_4Br_2 = \begin{matrix} C_6H_5{\cdot}CO \\ COOC_2H_5 \end{matrix}\!\!>\!CH{\cdot}CH_2{\cdot}CH_2Br + NaBr.$$

$$\begin{matrix} C_6H_5{\cdot}CO \\ COOC_2H_5 \end{matrix}\!\!>\!CNa{\cdot}CH_2{\cdot}CH_2Br = \begin{matrix} C_6H_5{\cdot}CO \\ COOC_2H_5 \end{matrix}\!\!>\!C\!<\!\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} + NaBr.$$

The following are the principal reactions of benzoyltrimethylenecarboxylic acid:—

1. It combines with hydroxylamine forming an oxime, $C_{11}H_{11}NO_3$.

2. It is readily reduced by sodium amalgam with formation of hydroxybenzyltrimethylenecarboxylic acid, $\begin{matrix}C_6H_5\cdot CH(OH)\\ COOH\end{matrix}>C<\begin{matrix}CH_2\\ |\\ CH_2.\end{matrix}$

3. It is a saturated acid, and does not decolorise potassium permanganate in alkaline solution at ordinary temperatures even after standing for days.

4. When boiled with water, it is converted into benzoylpropyl alcohol:

$$\begin{matrix}C_6H_5\cdot CO\\ COOH\end{matrix}>C<\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + H_2O = C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH + CO_2.$$

5. On distillation, the acid yields benzoyltrimethylene with elimination of carbon dioxide:

$$\begin{matrix}C_6H_5\cdot CO\\ COOH\end{matrix}>C<\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} = C_6H_5\cdot CO\cdot CH<\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + CO_2.$$

Benzoyltrimethylene is a ketone, and as such it combines with hydroxylamine and phenylhydrazine. It dissolves readily in hydrobromic acid with formation of benzoylpropyl bromide:

$$C_6H_5\cdot CO\cdot CH<\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + HBr = C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2Br.$$

It will thus be seen that benzoyltrimethylenecarboxylic acid exactly resembles acetyltrimethylenecarboxylic acid in its reactions, and there can be no doubt the two acids are similarly constituted.

In following out this subject, it is, doubtless, somewhat difficult to accept the proposition that such simple reagents as hydrobromic acid, or such simple treatment as boiling with water or dilute acids, should be sufficient to split the trimethylene ring; and, again, it is remarkable that acetyltrimethylene and acetyltrimethylenecarboxylic acid should be reduced by powerful reducing agents, with disruption of the trimethylene ring; whereas the trimethylene di- and tri-carboxylic acids are not acted on even by a large excess of sodium amalgam.

These and other facts make it at once evident that the stability of the trimethylene ring in its derivatives depends very much on the nature and position of the substituting groups; thus, for instance, trimethylenedicarboxylic acid [1 : 2] and the tricarboxylic acid [1 : 2 : 3] are much more stable compounds than acetyltrimethylenecarboxylic acid or trimethylenedicarboxylic acid [1 : 1]. This is not

remarkable when it is borne in mind that in the case of the ethylene derivatives, the stability of the ring is very different in various compounds; thus, for instance, ethylene and acrylic acid (ethylenecarboxylic acid) readily combine with bromine and hydrogen bromide, whereas fumaric acid (ethylenedicarboxylic acid) is only with difficulty attacked by these reagents, and similarly some ethylene compounds readily take up water when treated with dilute sulphuric acid or sodium hydrate, whereas others are not attacked under these conditions. It appears to us that the apparent difficulties, which operate against the general acceptance of the trimethylene formula, are readily explained on the assumption that ethylene and trimethylene compounds are analogously constituted; both hydrocarbons may be represented as possessing free affinities, which in the case of ethylene unite between 2 carbon atoms, in the case of trimethylene between 3 carbon atoms, thus:—

$$\begin{matrix}-CH_2\\-CH_2\end{matrix} = \begin{pmatrix}CH_2\\CH_2\end{pmatrix}; \qquad \begin{matrix}-CH_2\\CH_2\\-CH_2\end{matrix} = \begin{pmatrix}CH_2\\CH_2\\CH_2\end{pmatrix}.$$

Owing to the slight difference in constitution, it is natural to suppose that such substances would in general possess somewhat similar, though not identical, properties; and if this view be accepted, there will then be no difficulty in explaining any of the above-mentioned reactions.

Preparation of Acetyltrimethylenecarboxylic Acid, $\begin{matrix}CH_2\\CH_2\end{matrix}\!>\!C\!<\!\begin{matrix}CO\cdot CH_3\\COOH\end{matrix}$.

The preparation of pure acetyltrimethylenecarboxylic acid is a matter of considerable difficulty, and as we required this substance in large quantities for subsequent experiments, it was thought necessary to work out some method by which the acid could be readily and rapidly purified. The following was ultimately found to give satisfactory results.

Crude acetyltrimethylenecarboxylic acid (prepared by the hydrolysis of the crude ethereal salt boiling between 185—200° (see Trans., 1887, **51**, 829) is dissolved in water (10 grams of acid in 200 c.c. of water) rendered distinctly alkaline by the addition of baryta-water, heated to boiling, and a stream of carbonic acid passed through the liquid until the excess of baryta has been converted into carbonate.

By this treatment all traces of colouring matter and other impurities are removed, and the filtrate from the barium carbonate is found to be perfectly colourless. This filtrate is evaporated to a small bulk, filtered if necessary, acidified with dilute hydrochloric

acid, and repeatedly extracted with pure ether. The ethereal solution, after being dried over calcium chloride and evaporated, deposits a colourless oil. A sample of this was allowed to remain for three days over sulphuric acid in a vacuum and analysed, when it gave the following results:—

0·2671 gram substance gave 0·1551 gram H_2O and 0·5502 gram CO_2.

	Theory. $C_6H_8O_3$.	Found.
C.....	56·25 per cent.	56·19 per cent.
H.....	6·25 „	6·44 „
O.....	37·50 „	37·37 „

These numbers agree well with those required for acetyltrimethylenecarboxylic acid, and the acid thus purified was used in most of the subsequent experiments.

It is, nevertheless, obvious that any methyldehydropentonecarboxylic acid, $\begin{matrix}COOH\cdot C:C(CH_3)\\ \quad\quad\quad\

	Theory. $C_6H_8O_3$.	Found.
C	56·25 per cent.	55·91 per cent.
H	6·25 „	6·58 „
O	37·50 „	37·51 „

This acid is now completely free from methyldehydropentonecarboxylic acid, and appears to consist of practically pure acetyltrimethylenecarboxylic acid. Its most important property is that it is not affected by weak alkaline permanganate in the cold, a proof that the acid must be a saturated compound, as represented by the formula $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C<\begin{matrix}CO\cdot CH_3\\COOH\end{matrix}$, and that it cannot be vinylacetoacetic acid, $\begin{matrix}COOH\cdot CH\cdot CO\cdot CH_3\\|\\CH:CH_2\end{matrix}$, as suggested by Fittig (*Annalen*, **227**, 29), or methyldehydropentonecarboxylic acid, $\begin{matrix}CH:C(CH_3)\\|\\CH_2-CH_2\end{matrix}>O$, as suggested by Lipp (*Ber.*, **22**, 1210).

This important test for saturated compounds, which was devised by Baeyer (*Annalen*, **245**, 146), was, in the present case, carried out as follows:—2 drops of the acid were dissolved in an excess of a weak solution of potassium carbonate, in a test tube, and 1 drop of a weak permanganate solution added; the pink tint produced was permanent, even after standing for two days, whereas, if the acid had been unsaturated, the colour would, at once, have been discharged.

The properties of pure acetyltrimethylenecarboxylic acid are otherwise very similar to those of the crude acid previously described (Trans., 1885, **47**, 832).

Acetyltrimethyleneoxime, $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>CH\cdot C(NOH)\cdot CH_3$.

In some previous experiments on acetyltrimethylene (Trans., 1885, **47**, 835), it was stated that this substance combines with hydroxylamine to form a crystalline compound, probably an oxime; but this was not then analysed owing to lack of material. As, however, it was of great importance to establish the presence of a carbonyl group in acetyltrimethylene, these experiments were repeated on a larger scale, and a beautifully crystalline compound was obtained which, on examination, proved to be the desired oxime of acetyltrimethylene.

10 grams of pure acetyltrimethylene was dissolved in a little methyl alcohol, mixed with a concentrated aqueous solution of 12 grams of hydroxylamine hydrochloride, and a solution of 20 grams of pure potassium hydrate dissolved in methyl alcohol slowly run in

the whole being well cooled during the operation. After standing for 24 hours, water was added, the alcohol driven off by gently warming on a water-bath, the solution rendered slightly acid by the addition of dilute hydrochloric acid, and the whole extracted several times with pure ether. The ethereal solution, when dried over calcium chloride and evaporated, deposited a colourless oil which, on standing over sulphuric acid in a vacuum, almost completely solidified. The crude product was freed from oily mother liquor by spreading it on a porous plate, and then recrystallised from benzene. The following results were obtained on analysis :—

0·1451 gram substance gave 0·1239 gram H_2O and 0·3237 gram CO_2.

0·1774 gram substance gave 23·2 c.c. N ; $t = 11°$; bar. = 716 mm.

$CH_2<\begin{matrix}CH_2\\|\\CH_2\end{matrix}>CH\cdot C(NOH)\cdot CH_3$.

	Theory.	Found.
C.....	60·60 per cent.	60·84 per cent.
H.....	9·09 ,,	9·48 ,,
N.....	14·14 ,,	14·60 ,,

Acetyltrimethyleneoxime melts at 50—51°, and when carefully heated distils without decomposition; the oily distillate solidifies completely on rubbing it with a glass rod.

It is readily soluble in water, alcohol, ether, chloroform, benzene, and light petroleum, and can be obtained in the form of magnificent, glistening prisms by allowing its concentrated solution in cold benzene to evaporate spontaneously.

In an interesting paper on the decomposition of amylene nitrosate with sodium ethoxide (*Annalen*, **262**, 339—354), Wallach describes an oxime of the formula C_5H_9NO, which is isomeric with acetyltrimethyleneoxime. This oxime melts at 45°, and when heated with dilute sulphuric acid yields a new ketone, C_5H_8O, which boils at 98—102°.

From its method of formation, it is possible that this ketone, which is isomeric with acetyltrimethylene, has the constitution $CH_2<\begin{matrix}CH_2\\|\\CH_3\end{matrix}>C\cdot CO\cdot CH_3$.

Oxime of Acetopropyl Alcohol, $CH_3\cdot C(NOH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$, *and its Anhydride*, $CH_3\cdot\begin{matrix}C\\\|\\N-O-\end{matrix}\cdot\begin{matrix}CH_2\\|\\CH_2\end{matrix}$.

In the course of this investigation it became necessary, for reasons stated in the introduction, to prove that the anhydride of the oxime

of acetopropyl alcohol was not identical with the oxime of acetyltrimethylene (p. 866); and with this object in view we first prepared the oxime of acetopropyl alcohol.

3 grams of pure acetopropyl alcohol was dissolved in a little water, mixed with 3 grams of hydroxylamine hydrochloride, a moderately strong solution containing 5 grams of pure potassium hydrate added, and the whole allowed to remain at the ordinary temperature for three days. The product was then rendered slightly acid with hydrochloric acid, saturated with calcium chloride, and repeatedly extracted with ether; the ethereal solution was dried over calcium chloride, allowed to evaporate at the ordinary temperature, and the residual colourless oil left over sulphuric acid for four weeks.

The results obtained on analysis show that this substance is the oxime of acetopropyl alcohol:—

0·1935 gram substance gave 0·1659 gram H_2O and 0·3618 gram CO_2.

0·1660 gram substance gave 18·0 c.c. N; $t = 15°$; bar. = 726 mm.

	Theory. $C_5H_{11}NO_2$.	Found.
C	51·29 per cent.	51·00 per cent.
H	9·40 „	9·52 „
N	11·97 „	12·12 „

The oxime was readily converted into its anhydride by simply heating it on a watch glass at 100°.

The colourless, oily anhydride, which remained liquid even after standing over sulphuric acid in a vacuum for 14 days, gave on analysis the following numbers:—

0·1527 gram substance gave 0·1267 gram H_2O and 0·3381 gram CO_2.

0·0780 gram substance gave 9·7 c.c. N; $t = 18°$; bar. = 746 mm.

	Theory. C_5H_9NO.	Found.
C	60·61 per cent.	60·39 per cent.
H	9·09 „	9·22 „
N	14·14 „	13·97 „

This anhydride is isomeric with acetyltrimethyleneoxime, which is crystalline, and melts at 50—51°.

Oxime of Acetyltrimethylenecarboxylic Acid, $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C<\begin{matrix}C(NOH)\cdot CH_3\\COOH\end{matrix}$.

This interesting substance may be readily prepared in the following manner:—Acetyltrimethylenecarboxylic acid (1 mol.) is dis-

solved in a little water, mixed with a solution of pure potassium hydrate (4 mols.), and then a solution of hydroxylamine hydrochloride ($1\frac{1}{2}$ mols.) added, the temperature being kept below 30° during the operation. The product is allowed to stand for 24 hours, acidified with hydrochloric acid, the solution saturated with salt and repeatedly extracted with pure ether. The ethereal solution, after drying over calcium chloride, deposits the oxime, on evaporation, in beautiful, four-sided, tabular crystals.

The analysis of these crystals gave the following results:—

I. 0·2134 gram substance gave 0·1229 gram H_2O and 0·3933 gram CO_2.

0·2810 gram substance gave 23·2 c.c. N; $t = 15°$; bar. = 759 mm.

II. 0·1472 gram substance gave 0·0872 gram H_2O and 0·2714 gram CO_2.

0·2895 gram substance gave 24·4 c.c. N; $t = 12°$; bar. = 739 mm.

	Theory. $C_6H_9NO_3$.	Found. I.	Found. II.
C	50·36 per cent.	50·27	50·40 per cent.
H	6·29 „	6·40	6·58 „
N	9·78 „	9·84	9·69 „

This beautiful substance melts at about 157—158° with decomposition and rapid evolution of carbon dioxide. It dissolves readily in water, alcohol, and ether, but is only sparingly soluble in benzene, chloroform, and light petroleum.

In view of the interest which attaches to the formation of internal anhydrides in the oximes of β-ketonic acids (see below), the stability of the oxime of acetyltrimethylenecarboxylic acid was further tested by heating the substance at 100° for half an hour. At the end of this time the oxime was found to be wholly unchanged in appearance and melting point, and the following analysis shows that no formation of anhydride had taken place.

0·213 gram substance gave 18·5 c.c. N; $t = 17°$; bar. = 739 mm.

	Theory. $C_6H_9NO_3$.	Found.
N	9·78 per cent.	9·86 per cent.

Similar results were obtained with the oxime of benzoyltrimethylenecarboxylic acid (p. 883).

The formation and stability of the oximes of acetyltrimethylenecarboxylic acid and benzoyltrimethylenecarboxylic acid are extremely

interesting in their relation to the recent work of Claisen (*Ber.*, **24**, 140) and of Hantzsch (*Ber.*, **24**, 495—506, and other papers) on the aldoximes and the oximes of ketonic acids.

Hantzsch explains the isomerism, so often observed in structurally identical oximes, such as in the case of benzaldoxime, $C_6H_5\cdot CH{:}NOH$, by assuming that these may exist in two stereochemical forms thus:—

$$\underset{\text{OH}\cdot\text{N}}{\overset{\text{C}_6\text{H}_5\cdot\text{CH}}{\overset{\|}{}}}, \qquad \underset{\text{N}\cdot\text{OH}}{\overset{\text{C}_6\text{H}_5\cdot\text{CH}}{\overset{\|}{}}}.$$

α-Aldoxime. *β*-Aldoxime.

The oximes of *β*-ketonic acids, however, according to Hantzsch, never appear in two stereochemical forms, and, indeed, so far, these have never been obtained in the free state. Thus, ethyl acetoacetate, when treated with hydroxylamine, yields methylisoxalone, the internal anhydride of the oxime of acetoacetic acid,

$$\text{CH}_3\cdot\text{C(NOH)}\cdot\text{CH}_2\cdot\text{COOH} = \overset{\text{CH}_3\cdot\text{C}\cdot\text{CH}_2\cdot\text{CO}}{\underset{\text{N}\text{---}\text{O}}{\overset{\|}{}\quad\quad\quad|}} + \text{H}_2\text{O}.$$

Similarly, benzoylacetic acid and hydroxylamine yield phenylisoxalone, $\overset{\text{C}_6\text{H}_5\cdot\text{C}\cdot\text{CH}_2\cdot\text{CO}}{\underset{\text{N}\text{---}\text{O}}{\overset{\|}{}\quad\quad\quad|}}$, and not the free oxime,

$$\text{C}_6\text{H}_5\cdot\text{C(NOH)}\cdot\text{CH}_2\cdot\text{COOH}$$

The formation of these anhydrides shows at once that the oximes of acetoacetic acid and of benzoylacetic acid have the *β*-configurations:

$$\underset{\text{N}\cdot\text{OH}}{\overset{\text{CH}_3\text{C}\cdot\text{CH}_2\cdot\text{COOH}}{\overset{\|}{}}}, \qquad \underset{\text{N}\cdot\text{OH}}{\overset{\text{C}_6\text{H}_5\cdot\text{C}\cdot\text{CH}_2\cdot\text{COOH}}{\overset{\|}{}}}.$$

The experiments on the oximes of acetyltrimethylenecarboxylic acid and of benzoyltrimethylenecarboxylic acid show conclusively that some of the oximes of *β*-ketonic acids, at all events, are capable of existing in the free state, and the fact that these oximes do not, even at 100°, yield internal anhydrides (isoxazolones) appears to show that these have the *α*-configuration,

$$\underset{\text{OH}\cdot\text{N}}{\overset{\text{CH}_3\cdot\text{C}\cdot\text{C(COOH)}<\text{CH}_2}{\overset{\|}{}\quad\quad\quad

Reduction of Acetyltrimethylenecarboxylic Acid.

As stated in the introduction, acetyltrimethylenecarboxylic acid is readily reduced by sodium amalgam with formation, in the first place, of hydroxyethyltrimethylenecarboxylic acid:

$$\begin{matrix}CH_3\cdot CO\\ COOH\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + H_2 = \begin{matrix}CH_3\cdot CH(OH)\\ COOH\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}.$$

If, however, a very large excess of sodium amalgam is employed, the ultimate product of the reaction is α-ethyl-β-hydroxybutyric acid, thus:—

$$\begin{matrix}CH_3\cdot CH(OH)\\ COOH\end{matrix}\!\!>\!C\!<\!\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + H_2 = CH_3\cdot CH(OH)\cdot CH(C_2H_5)\cdot COOH.$$

In studying this reduction, very carefully purified acetyltrimethylenecarboxylic acid was dissolved in water, neutralised with sodium carbonate, and reduced with nearly twice the calculated quantity of sodium amalgam (for H_2), added in small portions at a time. To promote thorough reduction, the vessel containing the sodium salt was constantly agitated, and the temperature prevented from rising by cooling externally by a stream of water.

As soon as the reduction was complete, the mercury was run off, the alkaline solution nearly neutralised with dilute hydrochloric acid, extracted with ether to remove a small quantity of a neutral substance which is always formed, acidified with hydrochloric acid, and extracted 10 times with pure ether.

The ethereal solution was dried over calcium chloride, evaporated, and the residual, almost colourless, oily acid, after standing over sulphuric acid in a vacuum for three days, analysed with the following result:—

0·1609 gram substance gave 0·1098 gram H_2O and 0·3296 gram CO_2.

0·1516 gram substance gave 0·1035 gram H_2O and 0·3089 gram CO_2.

	Theory. $C_6H_{10}O_3$.	Found. I.	Found. II.
C	55·38 per cent.	55·80	55·59 per cent.
H	7·69 „	7·58	7·59 „
O.....	36·92 „	36·62	36·82 „

Hydroxyethyltrimethylenecarboxylic acid is a thick, strongly acid syrup miscible with water in all proportions. It distils with very slight decomposition if rapidly fractioned under reduced pressure (30 mm.).

A small quantity of the acid used in Analysis II was very rapidly distilled under a pressure of 30 mm., and two fractions, 175—180° and 180—185°, collected. The first of these gave, on analysis, the following numbers, showing that there had been only a very slight loss of water during the distillation :—

0·1780 gram substance gave 0·1176 gram H_2O and 0·3630 gram CO_2.

	Theory. $C_6H_{10}O_3$.	Found.
C.....	55·38 per cent.	55·75 per cent.
H.....	7·69 „	7·38 „
N.....	36·92 „	36·87 „

The distilled acid was a thick, perfectly colourless oil, soluble in water with only a faint turbidity.

In order to prepare the *silver salt* of this acid, the two fractions referred to above were separately dissolved in small quantities of water, neutralised carefully with potassium hydrate, and mixed with a slight excess of silver nitrate, dissolved in a very small quantity of water. It is necessary to have all the solutions concentrated in the above operation, otherwise the silver salt, which is readily soluble in water, is not precipitated. The white silver salt, was then collected, washed with a little water, dried on a porous plate, and recrystallised twice from boiling absolute alcohol; it was thus obtained in the form of microscopic needles, which, on analysis, gave the following numbers :—

I. Silver salt from fraction of acid boiling at 175—180° (30 mm.)—
0·3912 gram substance gave 0·4330 gram CO_2, 0·1412 gram H_2O, and 0·1784 gram Ag.

II. Silver salt from fraction of acid boiling at 180—185° (30 mm.)—
0·4162 gram substance gave 0·4641 gram CO_2, 0·1446 gram H_2O, and 0·1894 gram Ag.

	Theory. $C_6H_9O_3Ag$.	Found. I.	Found. II.
C.....	30·38 per cent.	30·18	30·41 per cent.
H.....	3·80 „	4·01	3·86 „
Ag.....	45·58 „	45·61	45·50 „

The *copper salt* was obtained as a beautiful, green, crystalline mass, on adding a solution of copper sulphate to a strong, neutral solution of the potassium salt; it appears to contain 1 mol. H_2O :—

0·2714 gram substance gave, on ignition, 0·0682 gram of CuO.

	Theory. $(C_6H_9O_3)_2Cu + H_2O$.	Found.
Cu.....	20·10 per cent.	20·06 per cent.

This copper salt is readily decomposed by heating above 90°, and, therefore, the amount of water of crystallisation could unfortunately not be determined.

The *lead*, *barium*, and *calcium salts* of hydroxyethyltrimethylenecarboxylic acid are readily soluble in water.

α-Ethyl-β-hydroxybutyric Acid.—In order to determine whether sodium amalgam had any further action on hydroxyethyltrimethylenecarboxylic acid, the following experiment was instituted:—

11 grams of pure acetyltrimethylenecarboxylic acid was dissolved in water, neutralised with sodium carbonate, and reduced by the gradual addition of 500 grams of $2\frac{1}{2}$ per cent. sodium amalgam. The alkaline solution was neutralised with hydrochloric acid, evaporated to a small bulk, acidified, and the acid solution repeatedly extracted with ether. The ethereal solution was evaporated, the residual oily acid redissolved in sodium carbonate solution, and again treated with 500 grams of the amalgam. This operation was repeated a third time, and the ethereal solution of the ultimate product washed with a very little water, dried over calcium chloride, and evaporated.

The residual oily acid, after standing for some days over sulphuric acid in a vacuum, gave the following numbers on analysis:—

0·1748 gram substance gave 0·1440 gram H_2O and 0·3483 gram CO_2.

	Theory. $CH_3{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH$.	Found.
C	54·54 per cent.	54·35 per cent.
H.....	9·09 „	9·15 „
O	36·36 „	36·50 „

These numbers agree well with those required for *α-ethyl-β-hydroxybutyric acid*. This acid has already been prepared by Wahlschmidt (*Annalen*, **188**, 240) by the reduction of ethylic ethylacetoacetate with sodium amalgam:

$$CH_3{\cdot}CO{\cdot}CH(C_2H_5){\cdot}COOC_2H_5 + H_2 + NaOH = CH_3{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COONa + C_2H_5{\cdot}OH.$$

It is described as a syrup which, when distilled, is converted into α-ethylcrotonic acid, thus:—

$$CH_3{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH = CH_3{\cdot}CH{:}C(C_2H_5){\cdot}COOH + H_2O.$$

In order, therefore, to establish the identity of the acid obtained by the reduction of hydroxyethyltrimethylenecarboxylic acid with the

α-ethyl-β-hydroxybutyric acid obtained by Wahlschmidt, it was only necessary to submit the former to distillation, and thus to obtain α-ethylcrotonic acid, which, being a crystalline and well characterised acid, could readily be identified.

The sample of acid, analysed above, was, therefore, carefully distilled from a small retort, the distillate returned to the retort, and again distilled, the operation being repeated until it appeared that all the hydroxy-acid had been decomposed. The distillate was then dissolved in water, neutralised with sodium hydrate, and the solution, after extracting with ether to remove traces of neutral compounds, precipitated with acetate of lead. The white, crystalline lead salt, thus obtained, was purified by recrystallisation from water, the pure salt decomposed by hydrochloric acid, and the strongly-smelling, oily acid which separated extracted with ether. The ethereal solution was dried over calcium chloride and allowed to evaporate spontaneously, when a quantity of four-sided prisms separated out. The crystals melted at 38°, and showed all the properties of α-ethylcrotonic acid. Analysis :—

0·1320 gram substance gave 0·1051 gram H_2O and 0·3048 gram CO_2.

	Theory. $CH_3{\cdot}CH{:}C(C_2H_5){\cdot}COOH$.	Found.
C.....	63·16 per cent.	62·98 per cent.
H.....	8·77 „	8·85 „
O.....	28·07 „	28·17 „

In order to further establish the identity of this acid, the pure crystalline substance was dissolved in a slight excess of dilute sodium hydrate solution, which was then carefully neutralised with dilute nitric acid, heated to boiling, mixed with an excess of silver nitrate, and filtered. The solution, on cooling, deposited beautiful, white, glistening plates of silver α-ethylcrotonate.

The analysis of this salt gave the following result :—

0·2206 gram salt, on ignition, gave 0·1070 gram Ag.

	Theory. $CH_3{\cdot}CH{:}C(C_2H_5){\cdot}COOAg$.	Found.
Ag.....	48·87 per cent.	48·50 per cent.

These experiments prove, therefore, that the ultimate product of the action of sodium amalgam on acetyltrimethylenecarboxylic acid is *α-ethyl-β-hydroxybutyric acid.*

Reduction of Acetyltrimethylene.

Formation of Methylpropylcarbinol.

When reduced by means of sodium in moist ethereal solution, acetyltrimethylene takes up 4 atoms of hydrogen with formation of methylpropylcarbinol, thus:—

$$\begin{matrix}CH_2\\|\\CH_2\end{matrix}\!>\!CH\cdot CO\cdot CH_3 + 2H_2 = CH_3\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH_3.$$

At the same time a considerable quantity of a substance of high boiling point is produced which, on examination, proved to be dimethyl dipropyl glycol. This substance is probably formed thus:—

$$2\begin{matrix}CH_2\\|\\CH_2\end{matrix}\!>\!CH\cdot CO\cdot CH_3 + 3H_2 = \begin{matrix}CH_3\cdot CH_2\cdot CH_2\cdot C(OH)\cdot CH_3\\|\\CH_3\cdot CH_2\cdot CH_2\cdot C(OH)\cdot CH_3\end{matrix}.$$

The reduction was carried out as follows:—

15 grams of acetyltrimethylene was dissolved in 200 c.c. of ether, the solution floated on water, in a stout bottle connected with a reflux apparatus, and then 30 grams of sodium gradually added in small quantities at a time, the temperature being kept below 30° by sinking the bottle in water. As soon as the sodium had completely dissolved, the ethereal solution was separated, washed with a little water, dried over anhydrous potassium carbonate, and the ether slowly distilled off. The resulting, colourless, oily liquid was distilled, and thus readily separated into two principal fractions, about two-thirds passing over between 118° and 122° and the remainder between 210° and 230°. The lower fraction, on repeated fractionation, distilled constantly at 119·5°, and on analysis gave numbers agreeing with those required for methylpropylcarbinol, thus:—

0·1102 gram substance gave 0·2760 gram CO_2 and 0·1366 gram H_2O.

	Theory. $CH_3\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH_3$.	Found.
C	68·18 per cent.	68·30 per cent.
H	13·64 „	13·77 „
O	18·18 „	17·93 „

Methylpropylcarbinol has been prepared by Friedel (*Jahresbericht*, 1869, 513) from methyl propyl ketone and sodium amalgam, and by Markownikow (*J. Russ. Chem. Soc.*, **15**, 407) from zinc propyl and acetyl chloride. It boils at 118·5° under a pressure of 753·2 mm., and possesses properties exactly similar to those observed in our preparation.

In order to further establish the identity of the methylpropyl-

carbinol obtained from acetyltrimethylene, it was converted into its acetate by digestion with excess of acetic anhydride for two hours in a reflux apparatus. The product was then shaken up with cold water until the excess of acetic anhydride had been decomposed, the oily acetate extracted with ether, the ethereal solution washed with dilute sodium carbonate solution, and dried over calcium chloride; on evaporating the ether and distilling the residue, the whole passed over between 132° and 134°, and, on refractioning, the acetate was obtained pure as a colourless liquid boiling at 133·5°. The analysis gave the following results:—

0·1499 gram substance gave 0·1459 gram H_2O and 0·3539 gram CO_2.

	Theory. $CH_3\cdot CH(C_2H_3O_2)\cdot C_3H_7$.	Found.
C	64·61 per cent.	64·38 per cent.
H.....	10·77 „	10·81 „
O	24·62 „	24·81 „

The boiling point of this acetate is variously given as:—133—135° (Würtz, *Annalen*, **148**, 132); 130—135° (Friedel, *Zeit. für Chem.*, 1869, 476); 134—137° (Schorlemmer, *Annalen*, **161**, 269); these boiling points agree well with that found for the product from acetyltrimethylene.

Dimethyl Dipropyl Glycol.—The portion of the reduction product of acetyltrimethylene boiling at 210—230° was submitted to very careful fractionation in a Würtz flask with a long neck, and in this way a quantity of a thick, colourless oil was obtained boiling at 220—225°.

On analysis, it gave the following numbers:—

0·1142 gram substance gave 0·2881 gram CO_2 and 0·1282 gram H_2O.

	Theory. $\begin{matrix} C_3H_7\cdot C(OH)\cdot CH_3 \\ \vert \\ C_3H_7\cdot C(OH)\cdot CH_3 \end{matrix}$.	Found.
C	68·96 per cent.	68·81 per cent.
H.....	12·65 „	12·48 „
O	18·38 „	18·71 „

This substance appears to be identical with the methyl propyl pinacone obtained by Friedel (*Jahresbericht*, 1869, 513) by the reduction of methyl propyl ketone with sodium and water, and which this chemist found also to boil at 220—225°.

It was at first thought that this compound was ditrimethylene dimethyl glycol,

$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!CH\cdot C(OH)\cdot CH_3$$
$$\qquad\qquad\qquad\quad |$$
$$\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}\!\!>\!CH\cdot C(OH)\cdot CH_3 \quad ,$$

the formation of which could be readily understood; but this glycol contains C = 70·58 : H = 10·58 per cent. instead of C = 68·81 : H = 12·48, found above.

Action of Hydrogen Bromide on Acetyltrimethylene.

One of the most remarkable properties of trimethylenedicarboxylic acid is the ease with which it combines with hydrogen bromide, with formation of ω-bromethylmalonic acid, thus :—

$$\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C(COOH)_2 + HBr = CH_2Br\cdot CH_2\cdot CH(COOH)_2.$$

When subjected to the same treatment, acetyltrimethylene undergoes a perfectly similar decomposition, being converted into acetopropyl bromide, thus :—

$$\begin{matrix}CH_2\\|\\CH_2\end{matrix}>CH\cdot CO\cdot CH_3 + HBr = CH_2Br\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3.$$

In studying this interesting decomposition, 10 grams of pure acetyltrimethylene was added gradually to three times the volume of fuming hydrobromic acid (sp. gr. 1·83), care being taken to keep the temperature below 40°. After standing for 24 hours, the brownish solution was poured into water, the heavy oil which was deposited extracted twice with ether, and the ethereal solution washed with water, and dried over calcium chloride. On distilling off the ether, a brownish oil was obtained, which, on fractionation, boiled constantly at 120° under a pressure of 90 mm.

A bromine determination gave the following result, agreeing with that required for acetopropyl bromide :—

0·2134 gram substance, heated in a sealed tube with nitric acid and nitrate of silver, gave 0·2442 gram AgBr.

	Theory. $CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2Br$.	Found.
Br.....	48·50 per cent.	48·70 per cent.

Acetopropyl bromide has already been prepared by Colman and Perkin (Trans., **55**, 357) and by Lipp (*Ber.*, **22**, 1206) from acetopropyl alcohol and hydrobromic acid, and a careful comparison of the bromide from acetyltrimethylene with that obtained from acetopropyl alcohol showed that the two products were identical.

Hydrolysis of Acetyltrimethylene.

One of the most interesting reactions of acetyltrimethylenecarboxylic acid is the decomposition which it undergoes on prolonged

boiling with water, whereby it is resolved apparently quantitatively into acetopropyl alcohol and carbon dioxide (Trans., **51**, 829; **55**, 357), thus:—

$$\begin{matrix}CH_3\cdot CO\\ COOH\end{matrix}\!\!>\!C\!<\!\!\begin{matrix}CH_2\\ CH_2\end{matrix} + H_2O = CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH + CO_2.$$

In order to determine whether acetyltrimethylene,

$$CH_3\cdot CO\cdot CH\!<\!\!\begin{matrix}CH_2\\ CH_2\end{matrix}$$

(which is obtained from the above acid by the elimination of carbon dioxide), would be hydrolysed by water, a number of experiments carefully conducted under different conditions were instituted.

A quantity of pure acetyltrimethylene (b. p. 112—113°) was dissolved in water, and the solution allowed to stand at the ordinary temperature for two weeks; anhydrous potassium carbonate was then added, the oily layer which separated extracted with ether, dried over calcium chloride, and the residue which remained after distilling off the ether carefully fractioned in a Würtz flask fitted with a long neck. The whole distilled between 110° and 115°, leaving no appreciable residue, thus showing that water at ordinary temperatures has no action on acetyltrimethylene.

In the second experiment, acetyltrimethylene was heated with four times its volume of water in a sealed tube at 100° for two days, and the product treated as above; in this case also, practically, the whole of the acetyltrimethylene was recovered unchanged. Experiments subsequently made showed that acetyltrimethylene is not hydrolysed even when heated with water for two days at 130° or for 12 hours at 200°.

This fact is very interesting as demonstrating the remarkable difference in stability between acetyltrimethylene and its isomer, *methyldehydropentone*, $\begin{matrix}CH{:}C(CH_3)\\ CH_2\!-\!-\!CH_2\end{matrix}\!\!>\!O$ (see p. 880), as the latter, in contact with water at ordinary temperature, is rapidly converted into acetopropyl alcohol (p. 882).

In a research on acetopropyl alcohol, Lipp (*Ber.*, **22**, 1192) states that his so-called trihydromethylenefurfuran, $\begin{matrix}CH_2{:}C\cdot CH_2\cdot CH_2\\ O\!-\!-\!-\!-\!CH_2\end{matrix}$ (which boils at 110—111°, and is in all probability identical with acetyltrimethylene), when heated in a sealed tube with 5 per cent. hydrochloric acid at 100°, is converted into acetopropyl alcohol. As acetyltrimethylene is not hydrolysed by water alone, it was thought interesting to study its behaviour with 5 per cent. hydrochloric acid under the conditions employed by Lipp.

For this purpose, 20 grams of pure acetyltrimethylene was heated in a sealed tube with six times its volume of 5 per cent. hydrochloric acid for one hour at 100°, the product saturated with potassium carbonate, and then repeatedly extracted with pure ether. This ethereal solution, after drying over anhydrous potassium carbonate and evaporating, deposited an oil which, on distillation under reduced pressure (100 mm.), boiled between 140° and 150°, and on repeated fractionation, the greater portion passed over between 144 and 146°, and gave the following numbers on analysis :—

0·1598 gram substance gave 0·1397 gram H_2O and 0·3450 gram CO_2.

	Theory. $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$.	Found.
C	58·82 per cent.	59·05 per cent.
H	9·81 „	9·71 „
O	31·37 „	31·24 „

This experiment shows, therefore, that acetyltrimethylene, although not appreciably attacked by heating with water even at 200°, is readily hydrolysed by dilute hydrochloric acid at 100° with formation of acetopropyl alcohol, thus :—

$$CH_3{\cdot}CO{\cdot}CH<\begin{matrix}CH_2\\|\\CH_2\end{matrix} + H_2O = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

Methyldehydropentonecarboxylic Acid, $COOH{\cdot}C{:}C(CH_3)>O$ (with $CH_2\cdot CH_2$).

This acid is apparently always present in the crude acetyltrimethylenecarboxylic acid prepared by hydrolysing the ethereal salt boiling between 180° and 210°, obtained as the principal product in the action of ethylene bromide on ethyl sodacetoacetate. The amount of methyldehydropentonecarboxylic acid present in this product appears to vary very considerably, and in spite of repeated experiments, we have only on one occasion been successful in obtaining this beautiful substance in any quantity in a pure condition.

The conditions employed in this experiment were approximately the following :—

During the preparation of very large quantities of ethyl acetyltrimethylenecarboxylate, a quantity of crude ethylene bromide and ethyl acetoacetate had been recovered as a fraction boiling between 120° and 185°, and weighing considerably over 1 kilo. This was fractioned once or twice, and thus separated into two principal fractions, boiling respectively at 130—150° and 170—185°. The former was considered to consist for the most part of ethylene bromide; the

latter contained large quantities of ethyl acetoacetate. These crude products were employed in preparing a fresh quantity of ethyl acetyltrimethylenecarboxylate, the actual amounts which came into operation being 560 grams of ethyl acetoacetate, 400 grams of ethylene bromide, 100 grams of sodium, and about 1200 grams of absolute alcohol.

The mixture prepared in the usual way (Trans., 1885, **47**, 829) was heated for five hours in a reflux apparatus, the alcohol distilled off as completely as possible, the residue mixed with water, and the oily ethereal salt extracted with ether. The oily residue obtained after distilling off the ether was then subjected to distillation in a rapid current of steam till no more oily drops came over with the condensed water, the distillate extracted with ether, and the ethereal solution dried over calcium chloride and evaporated. The residue was fractioned, and the portion boiling between 170° and 230° hydrolysed by boiling in a reflux apparatus with an alcoholic solution of 30 grams of potassium hydrate for four hours. The alcohol was distilled off, and the residue diluted with water and evaporated to a small bulk on a water-bath.

On standing, the liquid deposited beautiful, glistening plates of a potassium salt, which were dissolved by the addition of water, and the alkaline liquid acidified by hydrochloric acid, when a fine, white, crystalline mass was deposited. The crystals, which are very sparingly soluble in the salt solution, were collected, washed with a very little water, dried on a porous plate, and purified by recrystallisation from benzene. In this way the new acid was readily obtained pure in the form of brilliant, four-sided plates, which on analysis gave the following numbers:—

I. 0·1470 gram substance gave 0·0872 gram H_2O and 0·3041 gram CO_2.

II. 0·1614 gram substance gave 0·0922 gram H_2O and 0·3331 gram CO_2.

	Theory. $C_6H_8O_3$.	Found. I.	Found. II.
C	56·25 per cent.	56·41	56·28 per cent.
H	6·25 „	6·59	6·34 „
O	37·50 „	37·00	37·38 „

Methyldehydropentonecarboxylic acid melts at 150°, and at the same time decomposes into methyldehydropentone and carbon dioxide:

$$\begin{matrix} COOH\cdot C{:}C(CH_3) \\ | \quad\quad > O \\ CH_2\cdot CH_2 \end{matrix} = \begin{matrix} CH{:}C(CH_3) \\ | \quad\quad > O \\ CH_2 — CH_2 \end{matrix} + CO_2.$$

When heated carefully in a current of an indifferent gas, this acid sublimes in the form of feathery crystals, with only slight decomposition.

It is readily soluble in warm water, ether, alcohol, and benzene, but only sparingly in light petroleum and cold water. The solution in hot water deposits the acid in colourless needles, on cooling, but if the solution is boiled, rapid decomposition sets in, with evolution of carbon dioxide and formation of an oily neutral substance, which is obviously acetopropyl alcohol.

The basicity of methyldehydropentonecarboxylic acid was determined by titrating a known quantity of the pure acid with a standard solution of potassium hydrate.

0·4500 gram of acid required for neutralisation 35·4 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH) = 0·1978 gram KOH.

A monobasic acid of the formula $C_6H_8O_3$ requires 0·1950 gram KOH.

Methyldehydropentonecarboxylic acid differs from acetyltrimethylenecarboxylic acid very widely in its behaviour towards potassium permanganate. If a trace of the former acid is dissolved in a slight excess of dilute sodium carbonate solution, and a drop of permanganate solution added, the colour instantly disappears, and successive drops continue to be decolorised, until the acid is completely destroyed; acetyltrimethylenecarboxylic acid, on the contrary, does not decolorise permanganate solution.

Again, acetyltrimethylenecarboxylic acid, being a ketonic acid, reacts readily with hydroxylamine, yielding an oxime; methyldehydropentonecarboxylic acid is, on the other hand, not acted on by hydroxylamine. In order to prove this, 2 grams of the latter acid was dissolved in dilute potassium hydrate solution (containing 4 grams KOH), a solution of hydroxylamine hydrochloride (2 grams) added, and the whole allowed to stand for 24 hours. The aqueous solution was then concentrated, cooled well, acidified with hydrochloric acid, and the precipitate which separated collected, washed with a little water, and spread on a porous plate. The crystals, which weighed upwards of 1·7 grams and were free from nitrogen, were crystallised from benzene, and found to consist of unchanged methyldehydropentonecarboxylic acid.

Methyldehydropentone, $\begin{matrix} CH{:}C(CH_3) \\ | \\ CH_2{-}{-}CH_2 \end{matrix} > O.$

When heated above its melting point, methyldehydropentonecarboxylic acid is rapidly decomposed with evolution of carbon dioxide

and formation of methyldehydropentone. In order to obtain this very interesting substance in quantity, 20 grams of the pure dry acid was gently heated in a small retort placed in an oil-bath and connected with a well-cooled condenser, the distillate being collected in a small flask cooled by means of a freezing mixture. The limpid, ethereal-smelling oil thus obtained, on subsequent fractionation, boiled constantly at 82°, and consisted of pure methyldehydropentone. Analysis:—

I. 0·1311 gram substance gave 0·1171 gram H_2O and 0·3442 gram CO_2.

II. 0·0881 gram substance gave 0 0781 gram H_2O and 0·2295 gram CO_2.

	Theory. C_5H_8O.	Found. I.	Found. II.
C	71·42 per cent.	71·60	71·07 per cent.
H	9·52 „	9·67	9·85 „
O	19·05 „	18·73	19·08 „

Methyldehydropentone is isomeric with acetyltrimethylene, $CH_3{\cdot}CO{\cdot}CH<\begin{matrix}CH_2\\|\\CH_2\end{matrix}$ (b. p. 112°).

The specific gravity and magnetic rotation determinations of this substance, which were made by W. H. Perkin, sen., gave the following numbers:—

Density:—$d\,4°/4° = 0·9217$; $d\,10°/10° = 0·9154$; $d\,15°/15° = 0·9107$; $d\,20°/20° = 0·9062$; $d\,25°/25° = 0·9018$.

Magnetic Rotations.

	t.	Sp. rotation.	Mol. rotation.
	17·0°	1·0552	5·417
	17·0	1·0521	5·402
	17·0	1·0477	5·379
	17·4	1·0462	5·374
	17·8	1·0492	5·391
	14·3	1·0506	5·379
	12·7	1·0551	5·393
	12·8	1·0560	5·398
	12·0	1·0553	5·390
Average ..	15·3	1·0519	5·391

Action of Water on Methyldehydropentone. Formation of Acetopropyl Alcohol.

The formula given above to methyldehydropentone represents this substance as the anhydride of acetopropyl alcohol,

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH = CH_3{\cdot}C(OH){:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}OH = \begin{matrix} CH_3{\cdot}C{\cdot}O{\cdot}CH_2 \\ \| \quad\quad | \\ CH{\cdot}CH_2 \end{matrix} + H_2O.$$

It was, therefore, to be expected that this anhydride, when treated with water, would be converted into acetopropyl alcohol, just as methyldehydrohexone in contact with water is converted into acetobutyl alcohol (Trans., 1887, **51**, 724),

$$\begin{matrix} CH_3{\cdot}C{-}O{-}CH_2 \\ \| \quad\quad | \\ CH{\cdot}CH_2{\cdot}CH_2 \end{matrix} + H_2O = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

10 grams of methyldehydropentone and 50 c.c. of water were placed in a stoppered bottle and kept at the ordinary temperature for some days. The oily layer which floated on the top of the water gradually became less and less, and ultimately entirely disappeared; the reaction is much hastened by agitating and gently warming the bottle from time to time. The clear solution thus obtained was saturated with potassium carbonate, extracted 20 times with pure ether, the ethereal solution dried over potassium carbonate, evaporated, and the residual oil purified by distillation under reduced pressure (80 mm.). In this way a colourless oil was obtained, which boiled constantly at 139° and gave the following numbers on analysis:—

0·1548 gram substance gave 0·1388 gram H_2O and 0·3360 gram CO_2.

	Theory. $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$.	Found.
C	58·82 per cent.	59·19 per cent.
H	9·81 „	9·96 „
O	31·37 „	30·85 „

The substance produced by the action of water on methyldehydropentone is, therefore, acetopropyl alcohol, and in this respect methyldehydropentone differs widely from the isomeric acetyltrimethylene, which, as was shown on p. 877, is not acted on by water even at moderately high temperatures.

In a previous investigation of the products of the distillation of crude acetyltrimethylenecarboxylic acid (which, as has already been shown, always contains methyldehydropentonecarboxylic acid), a small quantity of a substance was obtained boiling at 85—95°, which, when dissolved in water, was converted into acetopropyl alcohol, and which, therefore, undoubtedly consisted of slightly impure methyldehydropentone (Trans., 1887, **51**, 831).

Lipp (*Ber.*, **22**, 1199) also described a substance boiling at 72—75°, which he obtained by distilling acetopropyl alcohol, and which should

therefore be the anhydride of the alcohol. It is probable that this substance, which, however, Lipp, curiously enough, describes as unstable, consisted of impure methyldehydropentone.

Oxime of Benzoyltrimethylenecarboxylic Acid,

$$\begin{matrix} C_6H_5\cdot C(NOH) \\ COOH \end{matrix} > C < \begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix}.$$

With the object of proving the ketonic nature of benzoyltrimethylenecarboxylic acid, and, at the same time, of demonstrating the similarity in constitution between this acid and acetyltrimethylenecarboxylic acid, experiments on the behaviour of this acid towards hydroxylamine were instituted. 1·9 grams of pure benzoyltrimethylenecarboxylic acid was dissolved in a dilute solution of potassium hydrate containing 2·2 grams of KOH; 1 gram of hydroxylamine hydrochloride in solution was added, and the mixture allowed to stand for 24 hours. The clear alkaline solution was acidified with hydrochloric acid, the sticky, semi-solid mass, which, on stirring with a glass rod, became quite solid, collected, washed with water, and dried on a porous plate. It was then ground up, extracted with a little boiling benzene to remove any unchanged benzoyltrimethylenecarboxylic acid and other impurities, and recrystallised from water. In this way thick, colourless prisms were obtained, which, on analysis, gave the following numbers:—

0·1474 gram substance gave 0·0768 gram H_2O and 0·3467 gram CO_2.

0·1436 gram substance gave 8·2 c.c. N; $t = 20°$; bar. = 755 mm.

	Theory. $C_{11}H_{11}NO_3$.	Found.
C	64·39 per cent.	64·15 per cent.
H	5·37 „	5·79 „
N	6·83 „	6·64 „

When heated in a capillary tube, the oxime softens at 160° and melts fairly sharply at about 164—166° with decomposition. The crystalline substance is readily soluble in alcohol and warm water, very readily in acetic acid, but only very sparingly in benzene, light petroleum, and chloroform.

The oxime of benzoyltrimethylenecarboxylic acid does not yield an anhydride, even on heating at 100° for one hour (compare pp. 868—869).

Reduction of Benzoyltrimethylenecarboxylic Acid.

Formation of Hydroxybenzyltrimethylenecarboxylic Acid,

$$\begin{matrix} C_6H_5\cdot CH(OH) \\ COOH \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH_2 \\ CH_2 \end{matrix}.$$

When subjected to the action of sodium amalgam, acetyl trimethylenecarboxylic acid is readily reduced with formation of hydroxyethyltrimethylenecarboxylic acid, and this acid, under the influence of a large excess of sodium amalgam, is ultimately reduced to α-ethyl-β-hydroxybutyric acid (see pp. 870 and 872).

The constitution of benzoyltrimethylenecarboxylic acid being analogous to that of acetyltrimethylenecarboxylic acid, it yields under similar circumstances hydroxybenzyltrimethylenecarboxylic acid,

$$\begin{matrix} C_6H_5\cdot CO \\ COOH \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH_3 \\ CH_2 \end{matrix} + H_2 = \begin{matrix} C_6H_5\cdot CH(OH) \\ COOH \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH_2, \\ CH_2 \end{matrix}$$

but whether this acid, on treatment with excess of sodium amalgam, can be converted into hydroxybenzylethylacetic acid,

$$C_6H_5\cdot CH(OH)\cdot CH\cdot(C_2H_5)\cdot COOH,$$

has not yet been definitely established. In studying this reduction, pure benzoyltrimethylenecarboxylic acid was dissolved in dilute sodium hydrate solution, and the sodium salt treated in a flat porcelain dish with about $1\frac{1}{2}$ times the calculated quantity of $2\frac{1}{2}$ per cent. sodium amalgam.

During the operation a white, crystalline sodium salt separated, which greatly impeded the reduction, and, therefore, especially at the latter part of the experiment, it was found necessary to bring this salt into solution by maintaining the liquid at a temperature of from 50—60°, with the occasional addition of small quantities of water The product, after being separated from the mercury, was filtered hot, acidified with dilute sulphuric acid, and several times extracted with ether. The ethereal solution, when dried over calcium chloride and evaporated, deposited a colourless oil, which rapidly and completely solidified on standing. The crystalline cake was purified first by recrystallisation from a mixture of benzene and light petroleum; the crystals were then dissolved in a small quantity of hot water, the solution filtered, and vigorously stirred as it cooled to prevent the formation of oily drops. In this way the new acid was obtained in the form of glistening, four-sided plates, which on analysis gave the following numbers:—

I. 0·1688 gram substance gave 0·0972 gram H_2O and 0·4238 gram CO_2.

II. 0·1472 gram substance gave 0·0868 gram H_2O and 0·3705 gram CO_2.

	Theory. $C_{11}H_{12}O_3$.	Found. I.	Found. II.
C	68·75 per cent.	68·49	68·57 per cent.
H	6·25 „	6·39	6·55 „
O	25·00 „	25·22	24·88 „

Hydroxybenzyltrimethylenecarboxylic acid melts at 94—96°. It is readily soluble in benzene, alcohol, and ether, but only moderately so in hot and sparingly in cold water.

The solution of the acid in dilute sodium carbonate does not decolorise potassium permanganate, even on standing for some time. When distilled, the acid is decomposed into water and a yellow oil. This oil appears to consist for the most part of two substances boiling at about 180—200° and 265—270° (140 mm.). The lower fraction smelt strongly of cinnamene, and the higher fraction on long standing solidified, but owing to the small quantities of these fractions at our disposal no clue to their constitution was obtained.

Salts of Hydroxybenzyltrimethylenecarboxylic Acid.

The *silver salt*, $C_{11}H_{11}AgO_3$, was prepared by precipitating a neutral solution of the ammonium salt with silver nitrate. The white, amorphous salt thus obtained was washed with water, dried on a porous plate over sulphuric acid in a vacuum, and analysed with the following result:—

0·2522 gram substance gave 0·0898 gram Ag.

	Theory. $C_{11}H_{11}AgO_3$.	Found.
Ag	36·03 per cent.	35·61 per cent.

A dilute neutral solution of the ammonium salt shows the following behaviour with reagents:—

Copper sulphate, a light blue precipitate, sparingly soluble in water. *Lead acetate*, a white, caseous precipitate, moderately soluble in hot water. *Zinc sulphate*, a white precipitate, soluble in hot water. *Barium chloride* and *calcium chloride*, no precipitate.

Reduction of Benzoyltrimethylene.

Formation of Phenylpropylcarbinol, $C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$.

The reduction of acetyltrimethylene to methylpropylcarbinol by means of sodium in moist ethereal solution is described on p. 874;

and, in studying this curious result, it appeared to us that it would be interesting to investigate the action of this reducing agent on benzoyltrimethylene, in order to determine whether both these ketones would behave in the same way under this treatment.

About 10 grams of pure benzoyltrimethylene dissolved in pure ether was floated on water, and reduced by 40 grams of sodium in small quantities at a time, the experiment being conducted exactly as in the case of the reduction of acetyltrimethylene. As soon as all the sodium had dissolved the ethereal solution was separated, washed with a little water, dried over calcium chloride, evaporated, and the coloured, oily residue purified by fractionation under reduced pressure (100 mm.). About half of the substance distilled between 165° and 175°, leaving a thick, oily residue, which did not distil without decomposition, and was, therefore, not further examined. The fraction 165—175°, on redistillation, passed over almost entirely between 168° and 170° (under a pressure of 100 mm.), and gave on analysis the following numbers:—

0·1589 gram substance gave 0·1246 gram H_2O and 0·4671 gram CO_2.

	Theory. $C_6H_5\cdot CH(OH)\cdot C_3H_7$.	Found.
C	80·00 per cent.	80·12 per cent.
H	9·33 „	9·33 „
O	10·66 „	10·55 „

The substance is obviously phenylpropylcarbinol, produced by the addition of 4 atoms of hydrogen to benzoyltrimethylene, thus:—

$$C_6H_5\cdot CO\cdot CH<\begin{matrix}CH_2\\ |\\ CH_2\end{matrix} + 2H_2 = C_6H_5\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot CH_3.$$

Phenylpropylcarbinol is a thick, colourless oil, of powerful aromatic odour, somewhat resembling that of benzyl alcohol.

Benzoylpropyl Alcohol, $C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$, *and Phenyldehydropentone*, $C_6H_5\cdot C{:}CH\cdot CH_2$ / $O — CH_2$.

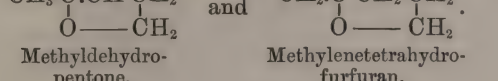
Unlike acetopropyl alcohol, benzoylpropyl alcohol is only theoretically capable of forming one internal anhydride, thus:—

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH = C_6H_5\cdot C(OH){:}CH\cdot CH_2\cdot CH_2\cdot OH =$$

$$C_6H_5\cdot C{:}CH\cdot CH_2 \;/\; O — CH_2 + H_2O,$$

Phenyldehydropentone.

whereas the former, on account of the presence of the methyl group, may yield two internal anhydrides :—



Methyldehydropentone. and Methylenetetrahydrofurfuran.

If now, on examination, the anhydride of benzoylpropyl alcohol should be found to be isomeric with benzoyltrimethylene, this fact would obviously be a very strong argument in favour of the trimethylene formula for the latter substance and its derivatives.

In order to decide this point, a quantity of finely-divided benzoyltrimethylenecarboxylic acid was converted into benzoylpropyl alcohol by boiling it with water for four days (see Freer and Perkin, Trans., 1887, **51**, 837), the hot solution filtered from a trace of an oily substance which had formed, rendered slightly alkaline by the addition of potassium carbonate, and the cold turbid liquid extracted several times with pure ether. The ethereal solution after drying over calcium chloride and evaporation, deposited an almost colourless oil which consisted apparently of almost pure benzoylpropyl alcohol. This oil, after removal of the last traces of ether by means of a current of air, gave the following numbers on analysis :—

0·1240 gram substance gave 0·0803 gram H_2O and 0·3348 gram CO_2.

	Theory. $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$.	Found.
C.....	73·17 per cent.	73·63 per cent.
H.....	7·32 „	7·19 „
O.....	19·51 „	19·18 „

When exposed over sulphuric acid in a vacuum, it is slowly but apparently completely converted into its anhydride (Freer and Perkin, *loc. cit.*).

On submitting crude benzoylpropyl alcohol to distillation, water is given off, and a small quantity of a colourless oil distils between 235° and 245°, leaving a considerable residue of high boiling point in the retort.

The fraction 235—245° thus obtained was dried over potassium carbonate, redistilled, and the portion boiling at 240—241° (750 mm.) analysed with the following result :—

0·1425 gram substance gave 0·0900 gram H_2O and 0·4273 gram CO_2.

	Theory. $C_6H_5\cdot C\cdot CH\cdot CH_2$ $O\text{——}CH_2$.	Found.
C.....	82·19 per cent.	81·77 per cent.
H.....	6·85 „	7·01 „
O.....	10·95 „	11·22 „

The substance is therefore phenyldehydropentone, the internal anhydride of benzoylpropyl alcohol. Phenyldehydropentone boils practically at the same temperature as benzoyltrimethylene (the latter boils at 239—239·5°, under a pressure of 720 mm.), and it is also very similar to it in appearance, odour, and many other properties. In order to determine whether the two substances were identical or isomeric, the action of hydroxylamine on both, under exactly similar conditions, was investigated.

2 grams of phenyldehydropentone was dissolved in methyl alcohol, mixed with a concentrated aqueous solution of 2 grams of hydroxylamine hydrochloride, a solution of 4 grams of potassium hydrate in methyl alcohol added, and the whole allowed to stand for 15 hours. After distilling off the methyl alcohol, the milky liquid was extracted three times with pure ether, the ethereal solution dried over calcium chloride and evaporated, and in this way about 1 gram of a colourless oil was obtained, which contained no nitrogen, and was most probably unchanged phenyldehydropentone. The alkaline solution, when acidified with hydrochloric acid, deposited an oil; this was extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the residual oil, which weighed about 1 gram, heated on a water-bath at 100° for one hour, and analysed with the following result:—

0·1249 gram substance gave 0·0840 gram H_2O and 0·3056 gram CO_2.

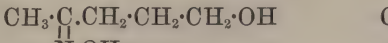
0·1823 gram substance gave 12·9 c.c. nitrogen; $t = 18°$; bar. = 7·45 mm.

	Theory. $C_{10}H_{13}NO_2$.	Found.
C.....	67·04 per cent.	66·71 per cent.
H.....	7·27 „	7·47 „
N.....	7·82 „	8·08 „

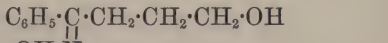
This substance is therefore the oxime of benzoylpropyl alcohol, $C_6H_5\cdot C(NOH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$, and the above experiment shows that phenyldehydropentone is itself incapable of forming an oxime, but that in contact with water and hydroxylamine it is slowly converted into the oxime of benzoylpropyl alcohol.

In view of the fact that the oxime of acetopropyl alcohol is entirely

converted into its anhydride on heating at 100°, it is very remarkable that the oxime of benzoylpropyl alcohol should remain unchanged at this temperature. This difference may, however, be readily explained, on the assumption that the oxime of acetopropyl alcohol has the β-configuration, that of benzoylpropyl alcohol the α-configuration, thus:—



(β). Oxime of acetopropyl alcohol.



(α). Oxime of benzoylpropyl alcohol.

This would be another example in support of Hantzsch's conclusions as to the structure of the ketoximes (*Ber.*, **24**, 31—36), namely, that the mixed aromatic ketoximes all have the α-configuration, whereas the aliphatic ketoximes, on the other hand, are β-oximes.

Further experiments are in progress on the oximes of acetopropyl alcohol and benzoylpropyl alcohol, and also on those of the corresponding butyl alcohols; these, it is hoped, will throw more light on this interesting point.

On studying the action of hydroxylamine on benzoyltrimethylene, using the same quantities and working under the same conditions as observed in the case of phenyldehydropentone, very different results from the above were obtained.

The product of the reaction, after distilling off the methyl alcohol, remained perfectly clear, and on acidifying with hydrochloric acid, a copious, oily precipitate was produced which in a short time became quite solid. The precipitate was collected, washed with water, dried on a piece of porous plate, and recrystallised several times from light petroleum and then from water. In this way the oxime of benzoyltrimethylene was obtained in hard, colourless crystals, which melted not very sharply at 90—92°, not at 86—87° as previously stated (Trans., 1885, **47**, 844).

The analysis of these crystals gave the following numbers:—

0·1745 gram substance gave 13·5 c.c. nitrogen; $t = 16°$; bar. = 745 mm.

	Theory. $C_6H_5\cdot C\cdot(NOH)\cdot CH<\begin{matrix}CH_2\\CH_2\end{matrix}$.	Found.
N.....	8·69 per cent.	8·84 per cent.

Considerable difficulty was experienced in obtaining this substance in a pure condition; it appeared to be a mixture of two compounds, and it is therefore possible that the oxime of benzoyltrimethylene exists in two modifications.

In view of the results obtained in these experiments, there can now

be no doubt that benzoyltrimethylene and phenyldehydropentone are totally different compounds.

Phenyl Tetramethylene Glycol, $C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, *and Phenyl Tetramethylene Dibromide*, $C_6H_5{\cdot}CHBr{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$.

In a previous investigation by P. C. Freer and one of us (Trans., 1887, **51**, 837), the action of water on benzoyltrimethylenecarboxylic acid at 100—110° was carefully studied, as it was thought that in this way benzoylpropyl alcohol might be obtained, thus:—

$$\begin{matrix} C_6H_5{\cdot}CO \\ COOH \end{matrix}\!>\!C\!<\!\begin{matrix} CH_2 \\ CH_2 \end{matrix} + H_2O = C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH + CO_2.$$

This decomposition would be analogous to the formation of acetopropyl alcohol from acetyltrimethylenecarboxylic acid by boiling it with water (Trans., 1887, **51**, 829). Although present in the aqueous solution obtained, it was not, at that time, found possible to isolate this ketone alcohol, owing to the fact that it decomposes at ordinary temperatures into water and its anhydride, methyldehydropentone, thus:—

$$C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH = \begin{matrix} C_6H_5{\cdot}C{:}CH{\cdot}CH_2 \\ O\text{——}CH_2 \end{matrix} + H_2O.$$

(For later experiments, see p. 887.)

In a subsequent investigation by Dr. Schloesser and one of us, these experiments were repeated, and on treating the aqueous solution of benzoylpropyl alcohol with sodium amalgam we obtained phenyl tetramethylene glycol, thus:—

$$C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH + H_2 = C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH,$$

and this, being much more stable than the ketone alcohol, could be isolated without difficulty in the usual way.

Pure benzoyltrimethylenecarboxylic acid was dissolved in ammonia, reprecipitated by dilute hydrochloric acid, and the finely-divided acid thus obtained boiled with a considerable quantity of water for about three days until the evolution of carbonic anhydride had entirely ceased. The warm aqueous solution was filtered from a very small quantity of phenyldehydropentone, which is always formed, and then treated in a flat dish with four times the calculated quantity of sodium amalgam ($2\frac{1}{2}$ per cent.) in small quantities at a time, carbonic anhydride being passed through the liquid during the reduction. The product was saturated with potassium carbonate, extracted several times with ether, the ethereal solution dried over calcium chloride, concentrated on a water-bath, and then allowed to evaporate spontaneously in a glass dish. In this way, the new glycol was obtained

in hard, crystalline crusts, which, after recrystallisation from ether, gave on analysis the following numbers :—

0·1736 gram substance gave 0·1326 gram H_2O and 0·4594 gram CO_2.

	Theory. $C_{10}H_{14}O_2$.	Found.
C	72·17 per cent.	72·21 per cent.
H	8·44 „	8·48 „
O	19·28 „	19·23 „

Phenyl tetramethylene glycol melts at 75°. It is readily soluble in alcohol, ether, and hot water, but only sparingly in cold water. When heated at a high temperature, it is decomposed, water is split off, and a thick, colourless oil distils which is probably phenyl tetramethylene oxide, $C_6H_5\cdot CH\cdot CH_2\cdot CH_2$ / $O\text{———}CH_2$.

Phenyl Tetramethylene Dibromide.—Phenyl tetramethylene glycol is readily acted on by fuming hydrobromic acid at 100° with formation of a thick, oily substance which appears to be a mixture of the monobromhydrin of phenyl tetramethylene glycol with phenyl tetramethylene dibromide, but all attempts to isolate the pure dibromide from this mixture were unsuccessful. Ultimately the following method of preparing this substance, which is almost identical with that employed by Kipping and Perkin in the preparation of phenyl pentamethylene dibromide (Trans., 1890, **57**, 314), and gives a good yield of the almost pure product, was adopted. The pure glycol dissolved in chloroform is treated with $1\frac{1}{2}$ times the calculated quantity of phosphorus pentabromide in small quantities at a time at ordinary temperatures until all action has ceased. The solution is then decanted from any undecomposed pentabromide, washed well with water, dried over calcium chloride, evaporated on a water-bath, and the last traces of chloroform removed by exposure over paraffin under reduced pressure. In this way, a thick, almost colourless oil is obtained which on analysis gave the following numbers :—

0·2010 gram substance, heated at 180° with nitric acid and nitrate of silver, gave 0·2560 gram AgBr.

	Theory. $C_{10}H_{12}Br_2$.	Found.
Br.....	54·80 per cent.	54·18 per cent.

Phenyl tetramethylene dibromide is a very thick, almost colourless oil which on standing in the air gradually darkens.

Experiments on the Behaviour of Ethyl Acetyltrimethylenecarboxylate towards Isoamyl Iodide in the presence of Sodium Ethylate.

In studying the properties of ethyl trimethylenedicarboxylate, $\begin{matrix}CH_2\\|\\CH_2\end{matrix}>C(COOC_2H_5)_2$, it was found to behave in all respects as a disubstituted ethyl malonate derivative: that is, it was incapable of forming a sodium compound when treated with sodium ethylate; hence its constitution could not be represented by the formula $CH_2{:}CH{\cdot}CH(COOC_2H_5)_2$ (Trans., 1885, **47**, 821, and 1887, **51**, 849).

Now, if ethyl trimethylenedicarboxylate and ethyl acetyltrimethylenecarboxylate are similarly constituted, it follows that the latter should also be incapable of forming a sodium compound, a hypothesis which was fully borne out by experiment. Hence ethyl acetyltrimethylenecarboxylate cannot be represented by the formula $CH_2{:}CH{\cdot}CH<\begin{matrix}CO{\cdot}CH_3\\COOC_2H_5\end{matrix}$.

The experiment was conducted as follows:—

28 grams of pure ethyl acetyltrimethylenecarboxylate was mixed with sodium ethylate containing 4·2 grams of sodium, 64 grams of isoamyl iodide added, and the mixture heated for five hours on a water-bath in a flask connected with a reflux apparatus. After distilling off the alcohol as completely as possible, the residue was diluted with water, extracted several times with ether, the ethereal solution washed, dried over calcium chloride, and evaporated. A very small quantity of an ethereal oil was thus obtained; this, on fractionation, distilled principally between 195° and 210°, and consisted of slightly impure ethyl acetyltrimethylenecarboxylate; there was scarcely any residue boiling above 210° left in the retort.

The aqueous liquors were evaporated to expel alcohol, acidified with dilute sulphuric acid, and repeatedly extracted with ether. The ethereal solution was dried over calcium chloride and evaporated, when about 19 grams of an almost colourless oil remained, which, on examination, was found to consist of acetyltrimethylenecarboxylic acid. The crude acid was converted into the characteristic silver salt, and this, after recrystallisation, analysed with the following result:—

0·2367 gram substance gave on ignition 0·1083 gram silver.

	Theory. $\begin{matrix}CH_2\\\|\\CH_2\end{matrix}>C<\begin{matrix}CO{\cdot}CH_3\\COOAg\end{matrix}$.	Found.
Ag.....	45·89 per cent.	45·76 per cent.

This experiment proves that ethyl acetyltrimethylenecarboxylate is

incapable of forming a sodium compound which, when treated with isoamyl iodide, would yield a higher homologue, and, therefore, the constitution of this ethyl salt cannot be represented by the formula $CH_2{:}CH{\cdot}CH{<}^{CO{\cdot}CH_3}_{COOC_2H_5}$, as a substance of that constitution would, by such treatment, have been converted into ethyl isoamylvinylaceto-acetate, $^{CH_2{:}CH}_{C_5H_{11}}{>}C{<}^{CO{\cdot}CH_3}_{COOC_2H_5}$.

Action of Ethylene Bromide on the Sodium Compound of Ethyl Ethylacetoacetate.

In the preceding section of this paper, it was shown that attempts to introduce the alkyl radical isoamyl into the molecule of ethyl acetyltrimethylenecarboxylate were unsuccessful: the reason assigned being that, as a disubstituted ethyl acetoacetate derivative, this ethereal salt was incapable of forming a sodium compound which, when treated with an alkyl iodide, would yield higher homologues.

If this deduction be true, it follows that ethyl ethylacetoacetate, $CH_3{\cdot}CO{\cdot}CH(C_2H_5){\cdot}COOC_2H_5$, when treated with sodium and ethylene bromide, should also be incapable of yielding an ethyl substituted ethyl acetyltrimethylenecarboxylate. The following experiment was instituted with the object of testing this hypothesis:—

A mixture of 175 grams of ethyl ethylacetoacetate, 110 grams of ethylene bromide, and 26 grams of sodium (in the form of sodium ethylate) was heated for six hours on a water-bath, the alcohol then distilled off, water added, and the product extracted three times with ether. The ethereal solution was evaporated, and the oily residue submitted to distillation in a rapid current of steam, when it was found that almost the whole distilled over, leaving only a very small quantity of an oily residue in the retort. The distillate was extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the residual oil purified by fractional distillation. It was thus roughly separated into two fractions 120—200° (70 grams) and 200—240° (about 20 grams). The first portion, on careful repeated refractionation from a Würtz' flask provided with a long neck, yielded a large quantity of a colourless oil boiling constantly at 120°, and which, on examination, was found to consist of pure ethyl butyrate.

I. 0·1534 gram substance gave 0·3470 gram CO_2 and 0·1447 gram H_2O.

II. 0·1309 gram substance gave 0·2955 gram CO_2 and 0·1239 gram H_2O.

	Theory. $CH_3 \cdot CH_2 \cdot CH_2 \cdot COOC_2H_5$.	Found. I.	Found. II.
C	62·08 per cent.	61·69	61·57 per cent.
H	10·34 „	10·48	10·28 „
O	27·58 „	27·83	28·15 „

This ethereal salt was hydrolysed by boiling with potassium hydrate solution, and the acid obtained by acidifying the solution with hydrochloric acid and extraction with ether boiled constantly at 162—163°, and showed all the properties of normal butyric acid. The formation of ethyl butyrate in this reaction must be due to the partial hydrolysis of the ethyl ethylacetoacetate, brought about probably by the prolonged boiling of its sodium compound,

$$CH_3 \cdot CO \cdot CH(C_2H_5) \cdot COOC_2H_5 + H_2O = CH_3 \cdot COOH + CH_2(C_2H_5) \cdot COOC_2H_5.$$

The higher boiling fraction, obtained as described above, was submitted to most careful fractionation, but nothing definite could be isolated. The whole was therefore hydrolysed, and thus converted into a neutral substance (which was not examined), and a very small quantity of an oily acid.

As this acid might possibly have been an ethyl derivative of acetyltrimethylenecarboxylic acid, a number of experiments were instituted with the object of proving its identity. As, however, the substance was not attacked by fuming hydrobromic acid with formation of a substituted acetopropyl bromide, nor decomposed by boiling with water yielding a substituted acetopropyl alcohol, there can be no doubt that an acid constituted analogously to acetyltrimethylenecarboxylic acid was not present.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

The Synthetical Formation of Closed Carbon Chains. Part I (continued). *Action of Propylene Bromide on the Sodium Compounds of Ethyl Acetoacetate and Ethyl Benzoylacetate.*

By W. H. Perkin, Jun., Ph.D., F.R.S., and James Stenhouse.

The action of ethylene bromide on the sodium compounds of ethyl malonate, ethyl acetoacetate, and ethyl benzoylacetate has been made the subject of repeated investigation (Fittig, Roeder, *Ber.*, **16**, 372. Perkin, *Ber.*, **17**, 54; Trans., 1885, **47**, 801; 1887, **51**, 849. Freer and Perkin, Trans., 1887, **51**, 820. Colman and Perkin, Trans., 1889, **55**, 358. Marshall and Perkin, Trans., 1891, **59**, 853. Lipp, *Ber.*, **22**, 1210), and the results obtained in these researches have led to the conclusion that in all these cases trimethylene derivatives are formed.

During the course of these investigations, we have been carrying on parallel experiments on the action of propylene bromide on the sodium compounds of ethyl acetoacetate and ethyl benzoylacetate. Propylene bromide does not react with these compounds nearly so readily as ethylene bromide, and the result is that the yields obtained are exceedingly small; we have, therefore, in one or two cases, not been able to examine the products as fully as could have been desired.

The investigation of the products has, however, proved that, in every case, substances are found which have a constitution analogous to those obtained when ethylene bromide is employed.

The Action of Propylene Bromide on the Sodium Compound of Ethyl Acetoacetate.

Ethyl Acetylmethyltrimethylenecarboxylate [1, 2, 1],

$$\begin{matrix} CH_3{\cdot}CO \\ COOC_2H_5 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH{\cdot}CH_3 \\ CH_2 \end{matrix}.$$

A short account of this reaction, and of some of the products obtained, has already been published (Trans., 1885, **47**, 850).

In the present instance, the quantities employed in one operation were the following:—

Ethyl acetoacetate	208 grams.
Sodium	36·8 grams.
Absolute alcohol	450 grams.
Propylene bromide	160 „

The sodium was dissolved in the alcohol, the well-cooled solution of sodium ethylate thus obtained gradually mixed with the ethyl acetoacetate, care being taken to prevent any appreciable rise of temperature by cooling with water; the propylene bromide was then added, and the mixture transferred to soda-water bottles, and heated at 100° for six hours. The alcoholic solution was decanted from the cake of sodium bromide which had formed, the alcohol distilled off on a water-bath, the residue mixed with water and the washings from the soda-water bottles, and extracted four times with ether. The ethereal solution was well washed with water containing a few drops of hydrochloric acid, dried over calcium chloride, evaporated, and the residual thick oil, which weighed about 100 grams, submitted to fractional distillation.

Between 125° and 160° (A), a large quantity of a heavy, colourless oil, which weighed about 54 grams, and consisted for the most part of unchanged propylene bromide, passed over. The thermometer then rose rapidly to 190° (B), and the residue, on fractionation under reduced pressure (100 mm.), distilled almost entirely between 130° and 260° (C), leaving a dark-brown residue in the retort; this, on cooling, partially solidified, and consisted of impure dehydracetic acid. The fraction below 125°, which smelt strongly of ethyl acetate, was repeatedly distilled, as it appeared probable that this fraction might contain α- or β-bromopropylene, C_3H_5Br, but as the portion boiling at 45—65° did not decolorise bromine, it is evident that these substances are not formed in any appreciable quantity in this reaction.

The fraction 125—160° (A) was twice fractioned, and the portion boiling between 130° and 150°, and which consisted for the most part of propylene bromide, was employed in the decomposition of fresh quantities of ethyl acetoacetate. It should be mentioned that a quantity of propylene bromide passes over with the alcohol, when the crude product of the reaction is distilled from a water-bath as described above. This is easily recovered by diluting the alcoholic distillate with twice its volume of water, allowing the milky liquid to stand till clear, and then separating the heavy layer of propylene bromide.

The fraction 130—230° (C) was distilled under the ordinary pressure, all passing over below 240° (D) being collected, and the residue (E) reserved for subsequent treatment.

The fraction D was mixed with the fraction B, and submitted to repeated fractionation from a Würtz flask provided with a long neck; in this way it was approximately separated into crude ethyl acetoacetate (b. p. 175—190°) and crude ethyl acetylmethyltrimethylenecarboxylate (b. p. 190—225°). The latter fraction was again repeatedly distilled, and a small quantity of a colourless oil which boiled fairly constantly at 210—212° analysed with the following result:—

0·1611 gram substance gave 0·1215 gram H_2O and 0·3725 gram CO_2.

	Theory. $CH_3{\cdot}CO\rangle C\langle CH{\cdot}CH_3$; $COOC_2H_5 \quad\quad CH_2$	Found.	Previous analysis.
C	63·53 per cent.	63·06 per cent.	63·55 per cent.
H	8·24 „	8·38 „	8·42 „
O	28·23 „	28·56 „	28·03 „

The substance employed in the previous analysis boiled at 215—217° (720 mm.); and there can be no doubt that the product boiling about 215° consists of nearly pure ethyl acetylmethyltrimethylenecarboxylate, the difference in the boiling point observed in the several preparations being probably due to the substance containing varying quantities of the isomeric ethyl dimethyldehydropentonecarboxylate, $COOC_2H_5{\cdot}C{:}C(CH_3)\rangle O$; the composition of this oil being apparently very similar to that obtained in the action of ethylene bromide on the sodium compound of ethyl aceteoacetate, which has been proved to be a mixture of ethyl acetyltrimethylenecarboxylate and ethyl methyldehydropentonecarboxylate.

The yield of the ethereal salt obtained by the above method is very small, not more than 50 grams of the fraction 205—215° being produced from 1 kilo. of ethyl acetoacetate.

Acetylmethyltrimethylenecarboxylic Acid, $CH_3{\cdot}CO\rangle C\langle CH{\cdot}CH_3$; $COOH \quad\quad CH_2$.

This acid has been previously described and analysed (Trans., 1885, **47**, 851).

In order to obtain sufficient material for our experiments, the fraction of the ethereal salt boiling at 195—225° (preceding section), and which consists for the most part of ethyl acetylmethyltrimethylenecarboxylate, was hydrolysed by boiling with a considerable excess of alcoholic potash, the product filtered from the potassium carbonate which had separated during the operation (due to the hydrolysis of some ethyl acetoacetate present in the ethereal salt employed), the

residue washed with alcohol, the filtrate evaporated with the addition of water till free from alcohol, the solution filtered, cooled well, acidified with dilute sulphuric acid, and extracted 10 times with pure ether. The ethereal solution was dried over calcium chloride, evaporated, and the residual brownish oil, which smelt strongly of acetic acid, purified by conversion into the barium salt. For this purpose, the oil was dissolved in a considerable quantity of water, mixed with barium hydrate solution until strongly alkaline, heated to boiling, and a current of carbonic anhydride passed through the liquid until no further precipitation of barium carbonate took place. The product was filtered, the almost colourless solution evaporated to a fairly small bulk, cooled well, acidified with dilute hydrochloric acid, and extracted 10 times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited an almost colourless oil, which, after standing over sulphuric acid under reduced pressure for 24 hours, gave the following results on analysis:—

0·1460 gram substance gave 0·0973 gram H_2O and 0·3176 gram. CO_2.

	Theory. $CH_3{\cdot}CO\diagdown\ \diagup CH{\cdot}CH_3$ $COOH\diagup C\diagdown CH_2$	Found.	Previous analysis.
C	59·15 per cent.	59·32 per cent.	58·66 per cent.
H	7·05 „	7·40 „	7·52 „
O	33·80 „	33·28 „	33·82 „

This substance is, therefore, almost pure acetylmethyltrimethylenecarboxylic acid, and as such it was employed in the subsequent experiments. This acid is a moderately thick, almost colourless oil, which, in dilute sodium carbonate solution, decolorises potassium permanganate solution instantly, but if excess of potassium permanganate is added, the solution allowed to stand for one hour, the excess of permanganate destroyed, the alkaline solution acidified and extracted with ether, an oily acid is obtained, which no longer decolorises permanganate. This behaviour indicates that the original acid is a mixture of acetylmethyltrimethylenecarboxylic acid and of dimethyldehydropentonecarboxylic acid (compare Trans., 1891, **59**, 864).

Oxime of Acetylmethyltrimethylenecarboxylic Acid,

$$CH_3{\cdot}C(:NOH)\diagdown\ \diagup CH{\cdot}CH_3$$
$$COOH\diagup C\diagdown CH_2$$

Acetyltrimethylenecarboxylic acid, when treated with hydroxylamine in alkaline solution, readily yields an oxime (Trans., 1891,

59, 867), thus proving that it contains a carbonyl group, and as it was important to show that this acid and acetylmethyltrimethylenecarboxylic acid were similarly constituted, experiments on the action of hydroxylamine on the latter were instituted.

Acetylmethyltrimethylenecarboxylic acid (1 mol.) was dissolved in a little water, mixed with a moderately strong solution of potassium hydrate (5 mols.), a saturated aqueous solution of hydroxylamine (2 mols.) added, and the whole allowed to stand at ordinary temperatures for 24 hours. The product was acidified with dilute hydrochloric acid, extracted several times with ether, and the ethereal extract, after being dried over calcium chloride and evaporated to a small bulk, was transferred to a small dish and allowed to evaporate at the ordinary temperature. The crystals which separated were freed from oily mother liquor by spreading on a porous plate, dried over sulphuric acid under reduced pressure, and then ground up in an agate mortar with a small quantity of pure benzene. In this way a trace of a dark-coloured impurity was dissolved, and after filtering and washing with a little benzene, a colourless, crystalline residue was obtained, which consisted of the almost pure oxime of acetylmethyltrimethylenecarboxylic acid.

The solution of this substance in warm water, when filtered and allowed to stand, deposits the pure oxime in colourless plates, which, after drying first on a porous plate over sulphuric acid under reduced pressure, and then at 80°, gave the following numbers on analysis :—

0·1229 gram substance gave 0·0818 gram H_2O and 0·2416 gram CO_2.

0·1907 gram substance gave 14·6 c.c. N ; $t = 16°$; bar. = 745 mm.

	Theory. $C_7H_{11}NO_3$.	Found.
C.....	53·50 per cent.	53·61 per cent.
H	7·01 „	7·39 „
N	8·92 „	8·63 „

Acetylmethyltrimethylenecarboxylic acid oxime melts at 153—155° with decomposition. It is readily soluble in warm water and alcohol, but only sparingly in benzene, and is almost insoluble in light petroleum. It crystallises from water in beautiful, colourless, glistening plates.

Acetoisobutyl Alcohol, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2{\cdot}OH$, *and Acetoisobutyl Bromide*, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2Br$.

The action of water on acetyltrimethylenecarboxylic acid was first investigated by Freer and Perkin (Trans., 1887, **51**, 829), who showed

that, on prolonged boiling with water, it is decomposed into acetopropyl alcohol and carbonic anhydride, thus :—

$$\begin{matrix}CH_3\cdot CO\\ COOH\end{matrix}\!>\!C\!<\!\begin{matrix}CH_2\\ CH_2\end{matrix} + H_2O = CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH + CO_2.$$

That this was ω-acetyl normal propyl alcohol was subsequently proved by Colman and Perkin (Trans., 1888, **53**, 189) by oxidising the alcohol to levulinic acid.

Similarly, we have found that acetylmethyltrimethylenecarboxylic acid, under analogous conditions, is converted, apparently quantitatively, into an acetobutyl alcohol, thus :—

$$\begin{matrix}CH_3\cdot CO\\ COOH\end{matrix}\!>\!C\!<\!\begin{matrix}CH\cdot CH_3\\ CH_2\end{matrix} + H_2O = C_6H_{12}O_2 + CO_2.$$

The constitution of the resulting alcohol may be represented by either of the four following formulæ :—

I. $CH_3\cdot CO\cdot CH_2\cdot CH(CH_3)\cdot CH_2\cdot OH$. *Acetoisobutyl alcohol.*
II. $CH_3\cdot CO\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot CH_3$. *Acetopropylcarbinol.*
III. $CH_3\cdot CO\cdot CH(OH)\cdot CH(CH_3)_2$. *Acetoisopropylcarbinol.*
IV. $CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH_3$. *Acetoethylmethylcarbinol.*

Acetopropyl alcohol, obtained from acetyltrimethylenecarboxylic acid, is the normal primary alcohol, and as it is extremely probable that the corresponding ketone alcohol obtained from acetylmethyltrimethylenecarboxylic acid is analogously constituted, we shall assume, until evidence to the contrary has been deduced, that this ketone alcohol is acetoisobutyl alcohol,

$$CH_3\cdot CO\cdot CH_2\cdot CH(CH_3)\cdot CH_2\cdot OH.$$

The hydrolysis of acetylmethyltrimethylenecarboxylic acid was carried out by dissolving the acid in 20 times its weight of water, and heating the solution to boiling, in a flask connected with a reflux apparatus, for three days, at the end of which time the evolution of carbonic anhydride had practically ceased. The product was then concentrated by distillation from a flask connected with a long colonna until the greater bulk of the water had been removed, the residue saturated with potassium carbonate, and the turbid liquid, from which, on standing, the alcohol separated as a light, oily layer, extracted 20 times with pure ether. After drying over potassium carbonate and evaporating, a colourless oil was obtained, which, on distillation under reduced pressure, boiled constantly at 140—142° (100 mm.), and gave the following results on analysis :—

0·1478 gram substance gave 0·1393 gram H_2O and 0·3363 gram CO_2.

	Theory. $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2{\cdot}OH$.	Found.
C	62·07 per cent.	62·07 per cent.
H	10·34 „	10·49 „
O	27·59 „	27·44 „

Acetoisobutyl alcohol is a colourless liquid, which mixes in all proportions with water, and in its general properties bears a very close resemblance to acetopropyl alcohol and acetobutyl alcohol.

Acetoisobutyl alcohol dissolves in fuming hydrobromic acid with evolution of a considerable amount of heat, and formation of acetoisobutyl bromide, thus:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2{\cdot}OH + HBr = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2Br + H_2O.$$

After standing for some time, the product was poured into water, extracted three times with ether, the ethereal solution washed with water, dried over calcium chloride, evaporated, and the residual, yellowish oil distilled under diminished pressure (100 mm.). A considerable quantity of an almost colourless oil was thus obtained boiling at 135—140° (100 mm.), and, on analysis, gave numbers agreeing approximately with those required for acetoisobutyl bromide.

0·1601 gram substance, heated in a sealed tube with nitric acid and silver nitrate at 180° for four hours, gave 0·1625 gram AgBr.

	Theory. $C_6H_{11}BrO$.	Found.
Br	44·69 per cent.	43·18 per cent.

As in the case of acetobutyl bromide and acetopropyl bromide, this substance is evidently partially decomposed on distillation, with loss of hydrogen bromide, and this accounts for the analytical results coming too low.

Acetoisobutyl bromide is a thick, colourless oil, which, on standing, rapidly becomes dark coloured; it has a peculiar odour, closely resembling that of acetobutyl bromide or acetopropyl bromide.

Ethyl Methyldiacetyladipate,

$$\begin{matrix} CH_3{\cdot}CO \\ COOC_2H_5 \end{matrix} > CH{\cdot}CH(CH_3){\cdot}CH_2{\cdot}CH < \begin{matrix} CO{\cdot}CH_3 \\ COOC_2H_5 \end{matrix}.$$

When ethylene bromide reacts with the sodium compound of ethyl acetoacetate, one of the principal products of the reaction is ethyl

diacetyladipate (Trans., 1890, **57**, 205), and when propylene bromide is employed the reaction proceeds, in part, in a precisely similar manner, with formation of ethyl methyldiacetyladipate.

$$2\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CHNa + BrCH(CH_3)\cdot CH_2Br =$$
$$\begin{matrix}CH_3\cdot CO\\COOC_2H_5\end{matrix}\!>\!CH\cdot CH(CH_3)\cdot CH_2\cdot CH\!<\!\begin{matrix}CO\cdot CH_3\\COOC_2H_5\end{matrix} + 2NaBr.$$

In order to isolate this substance, the crude product of the action of propylene bromide on the sodium compound of ethyl acetoacetate after extraction with ether, as described on p. 68, was distilled in a current of steam until all the ethyl acetylmethyltrimethylenecarboxylate and unchanged ethyl acetoacetate and propylene bromide had passed over, and until only a very small quantity of oil came over with the condensed steam. The residual, thick, dark-brown oil, which showed properties very similar to those of crude ethyl diacetyladipate (*loc. cit.*, p. 216), was purified by conversion into the sodium compound in the following way:—

The oil, after extracting with ether, drying over calcium chloride, and evaporating, was weighed, dissolved in pure, dry ether, and gradually mixed with an excess of a solution of sodium ethylate, diluted with ether, and allowed to stand for a few minutes. The yellow, flocculent sodium compound, which separated, was collected, washed rapidly with ether, decomposed with dilute sulphuric acid, and the yellowish oil which is thus regenerated extracted with ether. The ethereal solution was then well washed with dilute sodium carbonate solution, dried over calcium chloride, and the conversion into the sodium compound repeated.

In this way a small quantity of a straw-coloured oil was obtained, which, after standing over sulphuric acid under reduced pressure for 24 hours, gave the following results on analysis:—

I. 0·1710 gram substance gave 0·1248 gram H_2O and 0·3802 gram CO_2.

II. 0·1496 gram substance gave 0·1073 gram H_2O and 0·3374 gram CO_2.

	Theory. $C_{15}H_{24}O_6$.	Found. I.	Found. II.
C	60·00 per cent.	60·63	61·50 per cent.
H	8·00 ,,	8·11	7·90 ,,
O	32·00 ,,	31·26	30·60 ,,

These numbers agree approximately with those required by the formula $C_{15}H_{24}O_6$.

Ethyl methyldiacetyladipate closely resembles ethyl diacetyladipate in its properties. In alcoholic solution it gives, with a drop of ferric chloride, an intense violet coloration; it combines readily with phenylhydrazine and, apparently, also with ammonia, but owing to the small amount of material at our disposal, these reactions were not further investigated.

Decomposition of Ethyl Methyldiacetyladipate by Heat.—When subjected to distillation under reduced pressure, ethyl diacetyladipate is decomposed with formation of a variety of substances, of which the most important are the following (Trans., 1890, **57**, 206):—

Ethyl methyldihydropentene-methylketonecarboxylate . $CH_3\cdot C(COOC_2H_5)\cdot CH\cdot CH_2\cdot C(CO\cdot CH_3)\cdot CH_2$.

Ethyl methyldihydropentene-dicarboxylate..... $CH_3\cdot C(COOC_2H_5)\cdot CH\cdot CH_2\cdot C(COOC_2H_5)\cdot CH_2$.

The first of these substances, on hydrolysis, yields methyldihydropentene methyl ketone, thus:—

$$CH_3\cdot C(COOC_2H_5)\cdot CH\cdot CH_2\cdot C(CO\cdot CH_3)\cdot CH_2 + 2KOH =$$
$$CH_3\cdot C(CH_2\cdot CH_2\cdot C(CO\cdot CH_3)\cdot CH_2) + K_2CO_3 + C_2H_5\cdot OH,$$

whereas the second, under similar conditions, is simply converted into the potassium salt of methyldihydropentenedicarboxylic acid, with elimination of alcohol, thus:—

$$CH_3\cdot C(COOC_2H_5)\cdot CH\cdot CH_2\cdot C(COOC_2H_5)\cdot CH_2 + 2KOH =$$
$$CH_3\cdot C(COOK)\cdot CH\cdot CH_2\cdot C(COOK)\cdot CH_2 + 2C_2H_5\cdot OH.$$

The decomposition of ethyl methyl diacetyladipate on distillation evidently proceeds in an exactly similar manner; but, in this case, owing to the presence of the additional methyl group, it is more difficult to assign the correct constitution to the substances formed.

On hydrolysing the product obtained by the distillation of crude ethyl methyldiacetyladipate, a neutral substance, $C_9H_{14}O$, and an acid, $C_9H_{12}O_4$, are obtained exactly as in the case of ethyl diacetyladipate. The neutral substance, which is obviously *dimethyldihydropentene methyl ketone* may have either of the following formulæ:—

I. $CH_3\cdot C(=CCO\cdot CH_3)\cdot CH_2\cdot CH(CH_3)\cdot CH_2$ or II. $CH_3\cdot C(=C\cdot CO\cdot CH_3)\cdot CH_2\cdot CH_2\cdot CH\cdot CH_3$,

and the constitution of the acid, which is clearly *dimethyldihydropentenedicarboxylic acid*, may be represented thus :—

I. $CH_3\cdot C(=C\cdot COOH)\cdot COOH\cdot CH\cdot CH(CH_3)\cdot CH_2$ or II. $CH_3\cdot C(=C\cdot COOH)\cdot COOH\cdot CH\cdot CH_2\cdot CH\cdot CH_3$.

Unfortunately, with the small amount of material at our disposal, we were not able to decide between these formulæ, but as we consider Formula I in each case to be the more probable, we have, for simplicity's sake, adopted them in this paper.

In carrying out these decomposition experiments, the crude product of the action of propylene bromide on the sodium compound of ethyl acetoacetate was fractioned as described on p. 68 until the thermometer rose to 190°, and the residue, which contains the ethyl methyldiacetyladipate, distilled under reduced pressure (100 mm.). The oil boiling at 130—230° (100 mm.) (C, p. 68), was repeatedly fractioned under reduced pressure, and in this way a straw-coloured oil was obtained in the form of two fractions boiling respectively at 208—211° and 212—215° (175 mm.).

These fractions gave, on analysis, the following numbers :—

I (208—211°). 0·1420 gram substance gave 0·1066 gram H_2O and 0·3432 gram CO_2.

II (212—215°). 0·1528 gram substance gave 0·1120 gram H_2O and 0·3684 gram CO_2.

	Found.	
	I.	II.
C	65·91	65·75 per cent.
H	8·34	8·14 „

The principal product of the distillation of ethyl diacetyladipate boiled constantly at 230—231° (200 mm.), and gave on analysis the following numbers as the mean of four experiments :—

C	62·93 per cent.
H	7·83 „

The difference between these numbers and those obtained above is amply accounted for by the introduction of an extra methyl group, and although the products in both cases are mixtures, there can be no

doubt, from the study of their behaviour on hydrolysis, that they are analogously constituted.

Dimethyldihydropentene Methyl Ketone, $CH_3 \cdot C \overset{CH_2 \cdot CH(CH_3) \cdot CH_2}{=\!=\!=} C \cdot CO \cdot CH_3$.

This substance is produced in considerable quantity by the hydrolysis of the crude ethereal salt boiling at 200—220° (175 mm.), obtained as explained in the previous section.

20 grams of this oil was digested with a moderately strong solution of 35 grams of potassium hydrate in absolute alcohol, in a flask connected with a reflux apparatus, for three hours on a water-bath. During the operation, a large amount of potassium carbonate separated, and the liquid became brownish, and acquired a strong odour of peppermint. The product was mixed with water, extracted five times with ether, the ethereal solution washed with water, dried over calcium chloride, evaporated, and the residual yellowish oil purified by fractional distillation. The principal fraction obtained was an almost colourless oil boiling at 195—205°, but a considerable residue was left in the retort which will be referred to again later on. The fraction 195—205° was again distilled, and the portion boiling at 198—200° analysed with the following result:—

I. 0·1570 gram substance gave 0·1444 gram H_2O and 0·4481 gram CO_2.

II. 0·1428 gram substance gave 0·1292 gram H_2O and 0·4070 gram CO_2.

	Theory. $C_9H_{14}O$.	Found. I.	Found. II.
C	78·26 per cent.	77·84	77·73 per cent.
H	10·15 „	10·21	10·05 „
O	11·60 „	11·95	12·22 „

Dimethyldihydropentene methyl ketone is a colourless oil, smelling strongly of peppermint, which, on standing in the light, rapidly decolorises, and it is remarkable that this oil, on repeated fractionation, sometimes yields a dark-brown distillate.

This behaviour is probably caused by the absorption of oxygen during the distillation, and this may be an explanation of the fact that one or two preparations of this ketone, on analysis, gave results considerably too low in carbon and slightly too low in hydrogen.

Dimethyldihydropentene methyl ketone in its general properties resembles closely the corresponding monomethyl derivative,

$$CH_3 \cdot C \overset{CH_2 \cdot CH_2 \cdot CH_2}{=\!=\!=} C \cdot CO \cdot CH_3,$$

obtained by the hydrolysis of ethyl diacetyladipate with alcoholic potash (Trans., 1890, **57**, 232) and by the action of dehydrating agents on diacetylbutane, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$ (Marshall and Perkin, Trans., 1890, **57**, 242).

It is isomeric with methyltetrahydrobenzene methyl ketone, $CH_2<\begin{matrix}CH_2{\cdot}C(CH_3)\\CH_2\ -\ CH_2\end{matrix}>C{\cdot}CO{\cdot}CH_3$, a substance produced by the action of dehydrating agents on diacetylpentane (Kipping and Perkin, Trans., 1890, **57**, 16), and which boils at 205—206°.

The thick, dark-brown oil boiling above 210° which remains in the retort after the above ketone has distilled over was collected from several operations, and distilled under reduced pressure (30 mm.); in this way a quantity of a thick, yellowish oil was obtained boiling at 230—240° (30 mm.). On analysis, it gave the following numbers:—

0·1638 gram substance gave 0·1540 gram H_2O and 0·5070 gram CO_2.

	Theory. $C_{18}H_{26}O$.	Found.
C	83·72 per cent.	84·41 per cent.
H	10·08 „	10·44 „
O	6·20 „	5·15 „

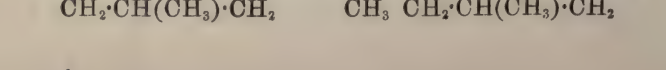
A determination of the molecular weight of this substance by Raoult's method, using acetic acid as the solvent, gave the following results:—

Substance taken.....	0·9828 gram.
Acetic acid taken	32·5 grams.
Melting point of the acetic acid ..	16·19°
Melting point of the mixture	15·73°
Depression of the melting point ..	0·46°
Molecular weight, $C_{18}H_{26}O$	258
Found	257

This substance has, therefore, the formula $C_{18}H_{26}O$, and is obviously produced by the condensation of 2 mols. of dimethyldihydropentene methyl ketone with the elimination of 1 mol. of water.

$$2C_9H_{14}O = C_{18}H_{26}O + H_2O.$$

Assuming this condensation to take place in the same way as the condensation of 2 mols. of acetone in forming mesityl oxide, the constitutiou of the substance $C_{18}H_{26}$ would be represented by the formula



Dimethyldihydropentene Methyl Ketoxime,

$$CH_3\cdot C \begin{array}{l} = \\ | \\ CH_2\cdot CH(CH_3)\cdot CH_2 \end{array} C\cdot C(:NOH)\cdot CH_3$$

In order to prepare this oxime, 5 grams of pure dimethyldihydropentene methyl ketone was dissolved in a little methyl alcohol, mixed with a solution of 12 grams of potassium hydrate dissolved in alcohol, a concentrated aqueous solution of hydroxylamine hydrochloride (5 grams) added, and the whole allowed to stand for 24 hours. The product was transferred to a porcelain dish, gently warmed on a water-bath till free from methyl alcohol, mixed with water, and the oil which separated extracted with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a colourless oil which, on fractionation under reduced pressure (100 mm.), distilled almost entirely between 172° and 176°.

A small quantity of the oil boiling at 175° (100 mm.) gave the following results on analysis :—

I. 0·1712 gram substance gave 0·1530 gram H_2O and 0·4436 gram CO_2.

0·1571 gram substance gave 13·1 c.c. N; $t = 20°$; bar. = 740 mm.

II. 0·1739 gram substance gave 0·1592 gram H_2O and 0·4469 gram CO_2.

	Theory. $C_9H_{15}NO$.	Found. I.	Found. II.
C	70·58 per cent.	70·66	70·08 per cent.
H	9·80 „	9·93	10·17 „
N	9·15 „	9·27	— „

Dimethyldihydropentene methyl ketoxime is a thick, pale-yellow oil, possessing the odour characteristic of oximes.

It is only sparingly soluble in cold, dilute, aqueous potassium hydrate, but dissolves readily in a moderately strong solution on warming, forming a colourless solution which, on cooling, deposits a white, crystalline potassium salt. This oxime is isomeric with orthomethyltetrahydrobenzene methyl ketoxime (Kipping and Perkin, Trans., 1890, **57**, 18).

Dimethylpentamethylenemethylcarbinol,

$$CH_3\cdot CH \begin{array}{l} - \\ | \\ CH_2\cdot CH(CH_3)\cdot CH_2 \end{array} CH\cdot CH(OH)\cdot CH_3$$

In studying the action of reducing agents on methyldihydropentene methyl ketone, Marshall and Perkin (Trans., 1890, **57**, 245)

found that this unsaturated ketone, when treated with sodium in moist ethereal solution, is not only converted into the carbinol, but that, under the influence of this powerful reagent, the double band in the ring is also reduced with formation of methylpentamethylenemethylcarbinol, thus :—

$$\begin{matrix} CH_3\cdot C \\ | \\ CH_2\cdot CH_2\cdot CH_2 \end{matrix} \!\!=\!\!=\!\!= \begin{matrix} C\cdot CO\cdot CH_3 \\ | \\ CH_2 \end{matrix} + 2H_2 = \begin{matrix} CH_3\cdot CH \\ | \\ CH_2\cdot CH_2\cdot CH_2 \end{matrix} \!\!-\!\!-\!\!- \begin{matrix} CH\cdot CH(OH)\cdot CH_3 \\ | \\ CH_2 \end{matrix}$$

Similar results were obtained by Kipping and Perkin in studying the action of reducing agents on orthomethyltetrahydrobenzene methyl ketone (Trans., 1890, **57**, 21).

This interesting point led us to experiment on the behaviour of dimethyldihydropentene methyl ketone when treated with sodium in moist ethereal solution; and we find that this ketone, under these conditions, also takes up 4 atoms of hydrogen with formation of dimethylpentamethylenemethylcarbinol.

About 15 grams of the pure ketone was dissolved in ether, the solution floated on a solution of sodium hydrate, and treated carefully with a very large excess of sodium, small quantities of water being added when necessary, and the reaction moderated by cooling the flask containing the mixture by a stream of water. During the operation, a quantity of a white sodium compound often separates, especially if the reduction is slowly conducted. This is obviously the sodium compound of the carbinol; it may be readily decomposed by the addition of water and gently agitating the flask. The ethereal solution was ultimately separated, washed with a little dilute hydrochloric acid, dried over calcium chloride, evaporated, and the residual almost colourless oil purified by repeated fractionation under reduced pressure.

The oil was thus separated into two substances, boiling respectively at 184—187° (100 mm.) and 230—240° (70 mm.).

The former of these gave, on analysis, the following numbers:—

0·1062 gram substance gave 0·1213 gram H_2O and 0·2970 gram CO_2.

	Theory.		Found.
	$C_9H_{18}O$.	$C_9H_{16}O$.	
C	76·07	77·14 per cent.	76·27 per cent.
H	12·67	11·43 „	12·69 „
O	11·27	11·43 „	11·04 „

This substance is, therefore, dimethylpentamethylenemethylcarbinol, $C_9H_{18}O$. It is a colourless, mobile oil, possessing an odour resembling that of menthol; when digested with acetic anhydride, it yields an acetate boiling at 200—202°.

The second substance, which is produced in small quantities during the reduction of the ketone, and boils at 230—240° (70 mm.), is a very thick, almost colourless oil; on standing, it showed no signs of crystallising.

It yielded the following numbers on analysis:—

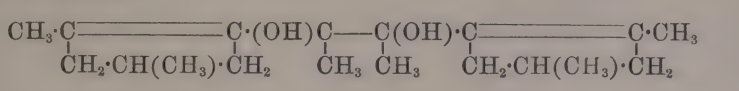
0·1212 gram substance gave 0·1220 gram H_2O and 0·3474 gram CO_2.

	Theory. $C_{18}H_{30}O_2$.	Found.
C	77·69 per cent.	78·17 per cent.
H	10·80 „	11·18 „
O	11·51 „	10·65 „

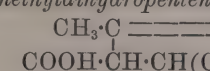
The molecular weight of this substance was determined by Raoult's method, using acetic acid as the solvent. The following results were obtained:—

Weight of substance taken.....	0·6676 gram
Weight of acetic acid	22·64 grams
Melting point of acetic acid	16·19°
Melting point of mixture.....	15·745°
Depression of the melting point.....	0·445°
Molecular weight, $C_{18}H_{30}O_2$.....	278
Found.....	258

This substance has therefore the formula $C_{18}H_{30}O_2$, and, from its mode of preparation and general properties, it is probably a pinacone of the formula



Dimethyldihydropentenedicarboxylic Acid,



The brownish alkaline solution from the hydrolysis of the oil, b. p. 200—205° (175 mm.), obtained by the distillation of ethyl methyldiacetyladipate, from which the crude dimethyldihydropentene methyl ketone had been extracted with ether, as described on p. 77, contains the potassium salt of dimethyldihydropentenedicarboxylic acid.

In order to isolate the acid, the alkaline solution was acidified with hydrochloric acid, extracted five times with ether, the ethereal solution dried over calcium chloride, evaporated, and the dark-

brownish, oily residue allowed to stand over sulphuric acid under reduced pressure for several days. As the oil showed no signs of crystallising, it was dissolved in a considerable quantity of water, mixed with barium hydrate solution until distinctly alkaline, heated to boiling, and a current of carbonic anhydride passed until the excess of barium hydrate had been removed. The product was filtered, the filtrate acidified with hydrochloric acid, extracted with ether, the ether evaporated, and the residue, which was much improved in appearance, again treated with barium hydrate as before. The ethereal extract ultimately obtained was dried over calcium chloride, evaporated, and the residual yellow oil allowed to stand over sulphuric acid, under reduced pressure, for some weeks, until it had almost completely solidified.

The crude substance was spread on a porous plate till free from oily impurity, recrystallised twice from water, and the straw-coloured, nodular masses thus obtained, after drying in a desiccator, analysed with the following result:—

0·1808 gram substance gave 0·1083 gram H_2O and 0·3905 gram CO_2.

	Theory. $C_9H_{12}O_4$.	Found.
C.....	58·69 per cent.	58·90 per cent.
H.....	6·52 „	6·65 „
O.....	34·79 „	34·45 „

Dimethyldihydropentenedicarboxylic acid melts at 180—182° with slight previous softening, and in its general properties bears a very close resemblance to methyldihydropentenedicarboxylic acid obtained from ethyl diacetyladipate (Trans., 1890, **57**, 233); the former was, however, found much more difficult to purify than the latter.

The basicity of dimethyldihydropentenedicarboxylic acid was determined by titration with standard potassium hydrate solution (1 c.c. = 0·00559 gram KOH).

0·2630 gram substance required for neutralisation 29·2 c.c. of potassium hydrate solution = 0·1632 gram KOH.

A bibasic acid of the formula $C_9H_{12}O_4$ requires 0·1600 gram KOH for neutralisation.

Action of Propylene Bromide on the Sodium Compound of Ethylbenzoylacetate. Formation of Ethyl Benzoylmethyltrimethylenecarboxylate,

$$\begin{matrix} C_6H_5\cdot CO \\ COOC_2H_5 \end{matrix}\!\!>\!C\!<\!\!\begin{matrix} CH\cdot CH_3 \\ | \\ CH_2 \end{matrix}.$$

It has been shown in previous researches (Trans., 1885, **47**, 836; 1887, **51**, 837; 1891, **59**, 833) that the sodium compound of ethyl

benzoylacetate, when treated with ethylene bromide at 100° in alcoholic solution, yields ethyl benzoyltrimethylenecarboxylate, thus:—

$$2C_6H_5\cdot CO\cdot CHNa\cdot COOC_2H_5 + C_2H_4Br_2 = \begin{matrix} C_6H_5\cdot CO \\ COOC_2H_5 \end{matrix}\!>\!C\!<\!\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} + C_6H_5\cdot CO\cdot CH_2\cdot COOC_2H_5 + 2NaBr.$$

This ethereal salt, on hydrolysis, yields the corresponding benzoyltrimethylenecarboxylic acid, which, when distilled, is converted quantitatively into benzoyltrimethylene with evolution of carbonic anhydride, thus:—

$$\begin{matrix} C_6H_5\cdot CO \\ COOH \end{matrix}\!>\!C\!<\!\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} = C_6H_5\cdot CO\cdot CH\!<\!\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} + CO_2.$$

While studying the action of propylene bromide on the sodium compound of ethyl acetoacetate, it occurred to us that it would be interesting to include the sodium compound of ethyl benzoylacetate in our investigations, and, as a result of our experiments, we find that the decomposition in this case takes place exactly as in the case of ethylene bromide, yielding derivatives of benzoylmethyltrimethylene.

78 grams of ethyl benzoylacetate was dissolved in a solution of 9·5 grams of sodium in 100 grams of alcohol, mixed with 80 grams of propylene bromide, and the mixture heated in soda-water bottles at 100° for three hours. The product was diluted with water, extracted four times with ether, the ethereal solution well washed, dried over calcium chloride, and the dark-brown, oily residue (73 grams) fractioned under reduced pressure (100 mm.).

In the first distillation, the following fractions were obtained:—

140—160°	about	28	grams.
160—210	„	11	„
210—230	„	25	„

The fraction 140—160° was found to consist principally of acetophenone; the fractions 160—230° contain, besides a little acetophenone, ethyl benzoylmethyltrimethylenecarboxylate and unchanged ethyl benzoylacetate. From these fractions, on repeated distillation, an oil (9 grams) was ultimately obtained boiling constantly at 223—226° (100 mm.); this, on analysis, gave the following numbers:—

I. 0·2100 gram substance gave 0·1304 gram H_2O and 0·5530 gram CO_2.

II. 0·1575 gram substance gave 0·0970 gram H_2O and 0·4138 gram CO_2.

	Theory. $C_6H_5\cdot CO\atop COOC_2H_5\!>\!C\!<\!\atop CH_2\cdot CH_3$	Found. I.	II.
C	72·41 per cent.	71·92	71·65 per cent.
H	6·89 „	6·89	6·84 „
O	20·69 „	21·19	21·51 „

It still contains traces of ethyl benzoylacetate, however, as is shown by the fact that a drop of the oil dissolved in a little alcohol gives a purple coloration with ferric chloride, and it is to the presence of traces of this substance that the slight deficiency in carbon found in the above analyses is due.

Ethyl benzoylmethyltrimethylenecarboxylate is an almost colourless oil which, when pure, appears to distil under ordinary pressures almost without decomposition; in its general properties, it bears a close resemblance to ethyl benzoyltrimethylenecarboxylate.

Benzoylmethyltrimethylenecarboxylic Acid, $C_6H_5\cdot CO\atop COOH\!>\!C\!<\!\atop CH_2\cdot CH_3$.

In order to prepare this acid, the pure ethereal salt (1 mol.) was digested with a moderately concentrated solution of potassium hydrate (2 mols.) in methyl alcohol for three hours, the solution diluted with water, evaporated on a water-bath till quite free from methyl alcohol, cooled well, filtered, acidified with dilute hydrochloric acid, and extracted three or four times with pure ether.

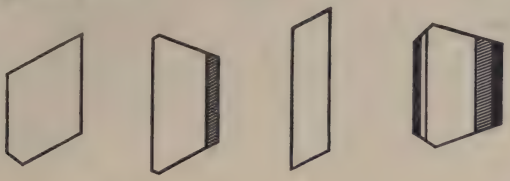
The ethereal solution was dried over calcium chloride, evaporated, and the residual yellow oil allowed to stand for some days. The crystals which formed were separated from the oily mother liquor by spreading on a porous plate, and the almost colourless residue washed as rapidly as possible with small quantities of ether on a filter pump. The beautiful, colourless, glistening, crystalline mass thus obtained, after drying over sulphuric acid under reduced pressure, gave the following results on analysis:—

0·1825 gram substance gave 0·1246 gram H_2O and 0·5503 gram CO_2.

	Theory. $C_6H_5\cdot CO\atop COOH\!>\!C\!<\!\atop CH_2\cdot CH_3$	Found.
C	70·59 per cent.	70·66 per cent.
H	5·88 „	6·04 „
O	23·53 „	23·30 „

Benzoylmethyltrimethylenecarboxylic acid melts at 128—129°, and at 140° it begins to decompose with evolution of carbonic anhydride.

It is readily soluble in alcohol and benzene, moderately soluble in ether and hot water, sparingly soluble in light petroleum and cold water. The solution of the acid in dilute sodium carbonate does not decolorise potassium permanganate even on long standing. The acid crystallises from its solution in warm water in curiously striated needles grouped together in stellate masses. On examination under the microscope, some of the more perfect crystals were found to have the following forms:—



The acid crystallises from a mixture of benzene and light petroleum in hard, colourless prisms, the surfaces of which are usually very striated and the edges uneven.

Oxime of Benzoylmethyltrimethylenecarboxylic Acid,

$$C_6H_5\cdot C(:NOH)\begin{matrix}\diagup\\ \diagdown\end{matrix}\!\!>C<\begin{matrix}CH\cdot CH_3\\ |\\ CH_2\end{matrix}$$
$$\qquad\qquad COOH$$

This substance is readily obtained by dissolving pure benzoylmethyltrimethylenecarboxylic acid in a large excess of aqueous potassium hydrate solution, adding twice the calculated quantity of hydroxylamine hydrochloride, and allowing the mixture to stand for two days. The product was warmed for a few minutes at 40—50°, cooled again, acidified with dilute hydrochloric acid, and the oxime, which separates at once in a solid condition, collected, washed with water, and spread on a porous plate. An analysis of the substance, dried over sulphuric acid under reduced pressure, gave the following numbers:—

0·1320 gram substance gave 7·6 c.c. N; $t = 16°$; bar. = 756 mm.

	Theory. $C_{12}H_{13}NO_3$.	Found.
N.....	6·39 per cent.	6·67 per cent.

The oxime prepared in this way melts at about 130—135° with decomposition. It is more readily soluble in hot water than the acid itself, but does not crystallise out well on cooling; it dissolves easily in ether and alcohol, but only sparingly in benzene and light petroleum. Unfortunately, owing to the very small amount of material at our disposal, we were not able to recrystallise this oxime, so that the melting point given above must be taken as approximate only.

Benzoylmethyltrimethylene, $C_6H_5\cdot CO\cdot CH<\begin{matrix}CH\cdot CH_3\\ |\\ CH_2\end{matrix}$.

When heated above 140°, benzoylmethyltrimethylenecarboxylic acid is gradually decomposed with evolution of carbonic anhydride and formation of benzoylmethyltrimethylene, thus:—

$$\begin{matrix}C_6H_5\cdot CO\\ COOH\end{matrix}>C<\begin{matrix}CH\cdot CH_3\\ |\\ CH_2\end{matrix} = C_6H_5\cdot CO\cdot CH<\begin{matrix}CH\cdot CH_3\\ |\\ CH_2\end{matrix} + CO_2.$$

In order to prepare this substance, the crude acid, prepared by hydrolysing crude ethyl benzoylmethyltrimethylenecarboxylate boiling at 210—235° (100 mm.), was distilled from a small retort, the distillate dissolved in ether, shaken once or twice with dilute sodium carbonate solution in order to remove benzoic acid, dried over calcium chloride, evaporated, and the residual almost colourless oil purified by fractionation under ordinary pressures. In this way a small quantity of a straw-coloured oil was obtained boiling at 240—245°, which, on analysis, gave the following numbers:—

0·1825 gram substance gave 0·1246 gram H_2O and 0·5503 gram CO_2.

	Theory. $C_{11}H_{12}O$.	Found.
C	82·50 per cent.	82·23 per cent.
H	7·50 „	7·64 „
O	10·00 „	10·13 „

Benzoylmethyltrimethylene is an almost colourless oil slightly soluble in boiling water; it boils at 240—245°, and in its general properties closely resembles benzoyltrimethylene, which boils at 239° (720 mm.).

Benzoyltrimethylene Oxime, $C_6H_5\cdot C(:NOH)\cdot CH<\begin{matrix}CH\cdot CH_3\\ |\\ CH_2\end{matrix}$.

In order to prepare this oxime, pure benzoylmethyltrimethylene was dissolved in methyl alcohol, mixed with a concentrated aqueous solution of $1\frac{1}{2}$ times the calculated quantity of hydroxylamine hydrochloride, and then four times the calculated quantity of a moderately strong solution of potassium hydrate in methyl alcohol slowly added.

After standing for 24 hours, the product was gently heated on a water-bath till free from alcohol, diluted with water, and extracted three times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited an almost colourless oil, which, even on long standing over sulphuric acid under reduced pressure, showed no signs of crystallising.

An analysis of this oxime gave the following numbers:—

0·2272 gram substance gave 15·7 c.c. N; $t = 17°$; bar. = 750 mm.

	Theory. $C_{11}H_{13}NO$.	Found.
N.....	8·00 per cent.	8·00 per cent.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

The Synthetical Formation of Closed Carbon Chains. Part II (continued). *Derivatives of Tetramethylene.*

By W. H. Perkin, Jun., Ph.D., F.R.S., and W. Sinclair, B.Sc.

In a former research (Trans., 1887, **51**, 1), it was shown that trimethylene bromide reacts with the sodium compound of ethyl malonate with formation of ethyl tetramethylenedicarboxylate:

$$2CHNa(COOC_2H_5)_2 + CH_2Br{\cdot}CH_2{\cdot}CH_2Br =$$
$$CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}>C(COOC_2H_5)_2 + CH_2(COOC_2H_5)_2 + 2NaBr.$$

This ethereal salt, on hydrolysis, yields the corresponding bibasic acid, which, when heated above its melting point, is decomposed with elimination of carbonic anhydride and formation of tetramethylenemonocarboxylic acid:

$$CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}>C(COOH)_2 = CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}>CH{\cdot}COOH + CO_2.$$

Owing to the formation of large quantities of ethyl pentanetetracarboxylate in the above reaction, the yield of tetramethylenecarboxylic acid obtained is so small that only those properties of the acid could be investigated which had a direct bearing on the question of its constitution.

During the course of some investigations on ethyl pentanetetracarboxylate, a considerable quantity of crude ethyl tetramethylenedicarboxylate accumulated, and we have taken this opportunity of studying the properties of tetramethylene derivatives more thoroughly.

Tetramethylenecarboxylic acid is characterised by extreme stability, and all previous experiments instituted with a view to

obtaining bromine and other substitution derivatives were unsuccessful.

Auwers and Bernhardi (*Ber.*, **24**, 2209) have lately studied the action of bromine on fatty acids in the presence of phosphorus (the so-called Hell-Volhard-Zelinsky method), and as the result of their experiments, these chemists are led to the conclusion that all acids which contain a hydrogen atom in the α-position readily form bromine substitution products, the bromine displacing the α-hydrogen atom.

As tetramethylenecarboxylic acid, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH\cdot COOH\end{matrix}$, contains a hydrogen atom in the α-position, we have investigated the action of bromine on this acid in the presence of phosphorus, and we find that by this means an almost quantitative yield of monobromotetramethylenecarboxylic acid, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CBr\cdot COOH\end{matrix}$, is obtained.

This acid has been very carefully investigated, as it appeared possible that under suitable conditions hydrogen bromide might be eliminated with formation of an unsaturated acid, $\begin{matrix}CH_2\cdot CH\\ CH_2\cdot C\cdot COOH\end{matrix}$, the study of which would yield very interesting results. When digested with aqueous potassium hydrate solution, the bromo-acid yields hydroxytetramethylenecarboxylic acid, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(OH)\cdot COOH\end{matrix}$, very little, if any, of an unsaturated acid being produced; the action of alcoholic potash or of sodium ethylate converts the bromo-acid into ethoxytetramethylenecarboxylic acid, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(OC_2H_5)\cdot COOH\end{matrix}$.

As these experiments did not lead to the desired result, our attention was turned to hydroxytetramethylenecarboxylic acid, because it was thought probable that dehydrating agents acting on this acid might remove the elements of water, forming the unsaturated acid, thus:—

$$\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(OH)\cdot COOH\end{matrix} = \begin{matrix}CH_2\cdot CH\\ CH_2\cdot C\cdot COOH\end{matrix} + H_2O.$$

Owing to the great stability of the hydroxy-acid, nothing but negative results have so far been obtained; sulphuric acid decomposes the acid with formation of *carbon monoxide*. Zinc chloride and other dehydrating agents convert the acid into high boiling products, and sodium acetate and acetic anhydride at 230° simply produce the corresponding acetate, $\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot C(OC_2H_3O)\cdot COOH\end{matrix}$.

Further experiments on this subject are in progress.

The reaction between ethylene bromide and the sodium compound of ethyl acetoacetate has repeatedly been made the subject of investigation, and the examination of the primary product of the reaction appears to leave no doubt that this substance is ethyl acetyltrimethylenecarboxylate, $\begin{matrix}CH_3\cdot CO\\ COOC_2H_5\end{matrix}>C<\begin{matrix}CH_2\\ CH_2\end{matrix}$, mixed with varying proportions of the isomeric ethyl methyldehydropentonecarboxylate, $COOC_2H_5\cdot C\begin{matrix}:C(CH_3)\\ CH_2\cdot CH_2\end{matrix}>O$.

Ethyl acetyltrimethylenecarboxylate, on hydrolysis, yields the corresponding acid; and this, on distillation, is converted into acetyltrimethylene, $CH_3\cdot CO\cdot CH<\begin{matrix}CH_2\\ CH_2\end{matrix}$, and carbonic anhydride; ethyl methyldehydropentonecarboxylate under similar conditions yields the isomeric methyldehydropentone, $\begin{matrix}CH:C(CH_3)\\ CH_2-CH_2\end{matrix}>O$. Similarly, ethyl benzoyltrimethylenecarboxylate is produced by the action of ethylene bromide on the sodium compound of ethyl benzoylacetate; in this case, however, no trace of the isomeric ethyl phenyldehydropentonecarboxylic acid appears to be formed; the free benzoyltrimethylenecarboxylic acid, on distillation, is converted quantitatively into carbonic anhydride and benzoyltrimethylene,

$$C_6H_5\cdot CO\cdot CH<\begin{matrix}CH_2\\ CH_2\end{matrix}.$$

Trimethylene bromide also reacts readily with the sodium compounds of ethyl acetoacetate and ethyl benzoylacetate, in both instances with formation of dehydrohexone derivatives, that is, of ethyl methyldehydrohexonecarboxylate, $\begin{matrix}CH_3\cdot C-O-CH_2\\ COOC_2H_5\cdot C\cdot CH_2\cdot CH_2\end{matrix}$ and ethyl phenyldehydrohexonecarboxylate, $\begin{matrix}C_6H_5\cdot C-O-CH_2\\ COOC_2H_5\cdot C\cdot CH_2\cdot CH_2\end{matrix}$, no trace of the isomeric tetramethylene derivatives being produced, and the acids obtained by the hydrolysis of these ethereal salts yield, on distillation, methyldehydrohexone, $\begin{matrix}CH_3\cdot C-O-CH_2\\ CH\cdot CH_2\cdot CH_2\end{matrix}$, and phenyldehydrohexone, $\begin{matrix}C_6H_5\cdot C-O-CH_2\\ CH\cdot CH_2\cdot CH_2\end{matrix}$, respectively.

As it is therefore not possible to obtain keto-derivatives of tetramethylene corresponding to acetyltrimethylene (trimethylene methyl ketone) and benzoyltrimethylene (trimethylene phenyl ketone) by this means, it appeared to us that it would be interesting to endeavour to prepare these substances from tetramethylenecarboxylic acid, in

order to be able to institute a direct comparison between the two series of ketones. The following are the results of our experiments:—

Tetramethylenecarboxylic chloride reacts very readily with zinc methide with formation of tetramethylene methyl ketone:

$$2\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot COCl\end{matrix} + Zn(CH_3)_2 = 2\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot CO\cdot CH_3\end{matrix} + ZnCl_2.$$

This interesting compound boils at 134°, or about 22° higher than trimethylene methyl ketone (b. p. 112°), and there is a considerable similarity between the two substances, those properties of the latter which are dependent on the instability of the trimethylene ring being naturally absent in the stable tetramethylene compound. In their behaviour towards reducing agents, for example, the two ketones differ widely. Trimethylene methyl ketone, when reduced by sodium in moist ethereal solution, is converted into propylmethylcarbinol (Trans., 1891, **59**, 874):

$$\begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!\!>\!CH\cdot CO\cdot CH_3 + 2H_2 = CH_3\cdot CH_2\cdot CH_2\cdot CH(OH)\cdot CH_3,$$

whereas tetramethylene methyl ketone, under precisely similar circumstances, yields the corresponding tetramethylenemethylcarbinol:

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot CO\cdot CH_3\end{matrix} + H_2 = \begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot CH(OH)\cdot CH_3.\end{matrix}$$

And, again, other reagents such as fuming hydrobromic acid and boiling dilute hydrochloric acid, which so readily decompose the trimethylene ring, appear to have no action whatever on tetramethylene methyl ketone.

This interesting point is again clearly brought out on comparing the properties of trimethylene phenyl ketone with those of tetramethylene phenyl ketone. The latter may be readily prepared by treating a solution of tetramethylenecarboxylic chloride in benzene with aluminium chloride, thus:—

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot COCl\end{matrix} + C_6H_6 = \begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot CO\cdot C_6H_5\end{matrix} + HCl.$$

It is a colourless oil boiling at 258—259°, or about 18° higher than the corresponding trimethylene phenyl ketone (b. p. 239—240°, 720 mm.). On reduction, it yields tetramethylenephenylcarbinol, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CH\cdot CH(OH)\cdot C_6H_5\end{matrix}$, whereas trimethylene phenyl ketone under similar conditions is converted into propylphenylcarbinol,

$C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$ (Trans., 1891, **59**, 885). In their behaviour towards fuming hydrobromic acid, again, these ketones differ widely, as, under these circumstances, trimethylene phenyl ketone yields benzoylpropyl bromide, $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$, whereas tetramethylene phenyl ketone is not acted on by this reagent.

Several other interesting compounds are described in this paper, and a special point has been made of the study of the magnetic rotation of the substances obtained.

The magnetic rotation and also the density determinations, which were made most carefully by W. H. Perkin, sen., have again proved most valuable as a means of discriminating between closed chain derivatives and unsaturated compounds, and they show in the clearest manner how very similar these tetramethylene compounds are to ordinary saturated compounds of the fatty series containing 2 atoms of hydrogen more.

Tetramethylenemonocarboxylic Acid, $\begin{matrix} CH_2{\cdot}CH_2 \\ | \quad\quad | \\ CH_2{\cdot}CH{\cdot}COOH \end{matrix}$.

The preparation and properties of this acid have been briefly described in a former communication (Trans., 1887, **51**, 1). In preparing large quantities of it, the following method has been found to give good results.

320 grams of ethyl malonate is dissolved in a cold solution of 46 grams of sodium in 550 grams of absolute alcohol, 210 grams of trimethylene bromide added, and the whole allowed to stand, in a capacious flask connected with a reflux apparatus, until the somewhat violent reaction which soon sets in has subsided. The product, which should be quite neutral, is heated on a water-bath until the bulk of the alcohol has distilled over, when the residue is mixed with water and extracted three times with ether; the ether is then evaporated, and the resulting thick oil, which consists of a mixture of ethyl tetramethylenedicarboxylate, ethyl pentanetetracarboxylate, and unchanged ethyl malonate, is subjected to rapid distillation in a current of steam until no more oily drops pass over with the condensed water. The distillate is extracted three times with ether, the ethereal solution dried over calcium chloride, evaporated, and the colourless, oily residue purified by fractional distillation.

The fraction 180—240° is hydrolysed by boiling with twice the calculated quantity of alcoholic potassium hydrate for two hours, the alcohol distilled off, the residue mixed with water, evaporated on a water-bath till quite free from alcohol, acidified, and extracted five times with pure ether. The ethereal solution is then dried over calcium chloride, evaporated, and the residual crude tetramethylene dicarboxylic acid distilled in quantities of about 50 grams at a time

and thus decomposed into carbonic anhydride and tetramethylenemonocarboxylic acid. The crude monobasic acid thus obtained is then further purified by fractional distillation, the portion boiling between 192° and 197° being used in subsequent experiments. The yield of tetramethylenemonocarboxylic acid obtained by this method is about 130 grams from 1 kilo. of ethyl malonate or about 40 per cent. of the theoretical yield. Freund and Gudeman (*Ber.*, **21**, 2694), using a slightly different method, state that they obtained only 8 per cent. of the theoretical yield.

In connection with this research, Dr. Walker has kindly determined the dissociation constants for the electrical conductivity of tetramethylenedicarboxylic acid and tetramethylenemonocarboxylic acid, with the following results:—

Tetramethylenedicarboxylic acid [1 : 1]..... K = 0·0834.
Tetramethylenemonocarboxylic acid ..... K = 0·00182.

It is interesting to note, as demonstrating the saturated nature of these substances, that solutions of the pure acids in sodium carbonate do not decolorise potassium permanganate even on long standing.

Tetramethylenecarboxylic Chloride, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot COCl\end{matrix}$

This substance, which has been obtained in small quantities by Freund and Gudeman (*Ber.*, **21**, 2696), is best prepared as follows:—

20 grams of the pure acid and 11 grams of freshly distilled phosphorus trichloride are heated by means of an oil-bath in a flask connected with a reflux condenser for half an hour, the temperature being so regulated that the mixture just boils. The product is carefully decanted from the layer of phosphorous oxide which forms, and twice fractioned. In this way, 20 grams of pure tetramethylenecarboxylic chloride are obtained boiling constantly at 137—139° (Freund and Gudeman give the boiling point as 142—143°); this, on analysis, gave the following result:—

0·2021 gram substance, heated with nitric acid and silver nitrate in a sealed tube at 150—160° for two hours, gave 0·2455 gram AgCl.

	Theory. C_5H_7OCl.	Found.
Cl	29·95 per cent.	30·07 per cent.

Monobromotetramethylenecarboxylic Acid, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CBr\cdot COOH\end{matrix}$

As stated in the introduction, this acid is readily prepared by acting on tetramethylenecarboxylic acid with bromine in the presence of

phosphorus. The apparatus employed in our experiments on the bromination of tetramethylenecarboxylic acid consisted of a round-bottomed flask of about 300 c.c. capacity, connected with a Liebig's condenser by means of a piece of stout rubber tubing stretched over the end of the condensing tube, and inserted into the neck of the flask so as to make a tight joint, and at the same time expose only a very small surface of india-rubber to the action of the bromine and hydrogen bromide vapours. A dropping funnel, fitted with a long delivery tube, was inserted loosely in the open end of the upright condenser.

50 grams of pure tetramethylenecarboxylic acid was mixed with 3 grams of dry amorphous phosphorus in the flask, and 150 grams of bromine added very slowly from the dropping funnel; the reaction took place at once with considerable evolution of heat, and much hydrogen bromide escaped from the end of the condenser. As soon as the whole of the bromine had been added (the operation takes about two hours), the flask was gently heated by means of a paraffin-bath for about three hours, the condenser was then removed, and the heating continued until all traces of bromine vapour had disappeared.

The heavy, dark-coloured, oily product was well cooled, poured into water, allowed to stand for 10 minutes, extracted three times with ether, the ethereal solution filtered from a few black specks which are usually present, washed with water, and carefully dried over calcium chloride. After distilling off the ether, a yellowish oil remained, which, on distillation under reduced pressure, passed over almost entirely between 150° and 155° under a pressure of 70 mm., as a colourless oil which, on standing, solidified to a mass of crystals. These were spread on a porous plate until the traces of oily mother liquor present had been entirely absorbed, dried over sulphuric acid under reduced pressure, and analysed with the following results:—

I. 0·2004 gram substance gave 0·0750 gram H_2O and 0·3467 gram CO_2.

0·4220 gram substance, heated with nitric acid and silver nitrate at 200° for three hours, gave 0·4392 gram AgBr.

II. 0·2810 gram substance gave 0·2930 gram AgBr.

	Theory. $C_5H_7BrO_2$.	Found. I.	Found. II.	
C	33·52 per cent.	33·57	—	per cent.
H	3·91 „	4·15	—	„
Br	44·70 „	44·25	44·40	„

Monobromotetramethylenecarboxylic acid melts at about 48—50°,

and the liquid, on cooling, solidifies to a mass of beautiful, colourless, pearly plates which have a faint butyric odour. It is readily soluble in alcohol, ether, and warm light petroleum, but only sparingly in water, although it is readily decomposed by boiling with this solvent with formation of hydrobromic acid. It dissolves readily in dilute aqueous potassium hydrate solution, and, on acidifying the solution, is deposited again as an oil. On boiling the alkaline solution, however, it is rapidly decomposed with formation of hydroxytetramethylenecarboxylic acid (p. 44). A crystal of the acid, placed on the surface of a dilute solution of sodium carbonate, rotates vigorously, and gradually dissolves; the solution of the sodium salt thus produced does not decolorise potassium permanganate, even on long standing.

The yield of the monobromo-acid obtained by the above method is very good; in two cases over 77 grams of the almost pure acid, boiling at 150—155° (70 mm.), was obtained from 50 grams of the tetramethylenecarboxylic acid, whereas theoretically it should have been 90 grams

Methyl Monobromotetramethylenecarboxylate, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CBr\cdot COOCH_3\end{matrix}$,

In the first experiments on the bromination of tetramethylenecarboxylic acid, the crude product of the action of bromine on 27 grams of the pure acid (see previous section) was poured into an excess of methyl alcohol instead of into water. The reason for this was that, as the methyl salt must boil at a very much lower temperature than the acid itself, it was thought that the salt would be less liable to decompose on distillation. After standing for about one hour, the methyl alcohol solution was poured into a large quantity of water, extracted with ether, the ethereal solution washed with water containing a little sodium carbonate, and then dried over calcium chloride. The ethereal solution, after being filtered from a small quantity of a black, flocculent impurity, was evaporated, and the residual, slightly-brownish oil, which weighed 51 grams, distilled under reduced pressure. Almost the whole passed over between 115° and 120°, under a pressure of 100 mm., and on repeated fractionation, the methyl salt was obtained pure as a colourless oil boiling constantly at 117—119° (100 mm.). The analysis gave the following numbers:—

0·1388 gram substance gave 0·0630 gram H_2O and 0·1867 gram CO_2.

0·2385 gram substance, treated with nitric acid and silver nitrate at 180—190° for three hours, gave 0·2739 gram AgBr.

	Theory. $C_6H_9BrO_2$.	Found.
C.....	37·31 per cent.	36·92 per cent.
H	4·67 „	5·04 „
Br.....	41·45 „	41·00 „

Methyl monobromotetramethylenecarboxylate is a heavy, colourless oil, which, when pure, may be distilled in small quantities under the ordinary pressure with only slight decomposition. The yield obtained by the above method is about 90 per cent. of the theoretical.

Hydroxytetramethylenecarboxylic Acid, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot C(OH)\cdot COOH\end{matrix}$.

This interesting acid is produced when monobromotetramethylenecarboxylic acid is boiled with aqueous potassium hydrate solution:

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CBr\cdot COOK\end{matrix} + KOH = \begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot C(OH)\cdot COOK\end{matrix} + KBr.$$

35 grams of the pure bromo-acid was dissolved in cold, moderately-dilute potassium hydrate solution, and heated to boiling in a flask connected with a reflux apparatus, small quantities of strong potassium hydrate being added from time to time in order to keep the liquid always distinctly alkaline. At the end of about two hours, the solution was evaporated to a fairly small bulk, acidified with dilute hydrochloric acid, and extracted at least 20 times with pure ether; the ethereal solution was then dried over calcium chloride, evaporated, and the residual thick, oily acid purified by distillation under reduced pressure (50 mm.). The thermometer rose rapidly to 140°, between which temperature and 155° a small quantity of a colourless oil passed over; but the greater portion distilled between 205° and 210°; the thermometer then rose rapidly to 260°, the last fraction becoming completely solid on standing. The fraction 205—210° gave, on analysis, the following numbers:—

0·2333 gram substance gave 0·1482 gram H_2O and 0·4414 gram CO_2.

	Theory. $C_5H_8O_3$.	Found.
C	51·72 per cent.	51·60 per cent.
H	6·90 „	7·06 „
O.....	41·38 „	41·34 „

Hydroxytetramethylenecarboxylic acid is a thick, colourless syrup, so thick that a test-tube containing a few grams of it may be inverted without the syrup falling out. It is miscible with water in all pro-

portions, and very difficult to completely extract from its aqueous solution by treatment with ether. The acid reduces ammoniacal silver solution very readily on warming, but not Fehling's solution even on boiling.

The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·9946 gram of the pure acid required for neutralisation 86 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH = 0·4807 gram KOH).

A monobasic acid of the formula $C_5H_8O_3$ requires 0·4804 gram KOH.

The salts of hydroxytetramethylenecarboxylic acid are almost all very readily soluble in water. Silver nitrate, copper, zinc, and lead acetates, barium and calcium chlorides give no precipitate with a moderately dilute neutral solution of the potassium salt. Hydroxytetramethylenecarboxylic acid dissolves in concentrated sulphuric acid with evolution of heat, and on standing a brisk effervescence takes place, due to the escape of *carbon monoxide*.

It is extremely probable that this remarkable phenomenon is due to the decomposition of the hydroxy-acid into formic acid ($CO + H_2O$) and ketotetramethylene, thus :—

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot C(OH)\cdot COOH\end{matrix} = \begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot CO\end{matrix} + H\cdot COOH.$$

A reaction of this nature would be exactly analogous to the formation of acetonedicarboxylic acid from citric acid (Pechmann, *Ber.*, **18**, 2289) and similar to that of cumalinic acid from malic acid (Pechmann, *Ber.*, **17**, 936) ; the first of these reactions takes place as follows :—

$$\begin{matrix}CH_2\cdot COOH\\ |\\ C(OH)\cdot COOH\\ |\\ CH_2\cdot COOH\end{matrix} = \begin{matrix}CH_2\cdot COOH\\ |\\ CO\\ |\\ CH_2\cdot COOH\end{matrix} + H\cdot COOH.$$

Owing to the small quantity of material at our disposal, this interesting decomposition has as yet not been further studied.

The yield of the distilled hydroxytetramethylenecarboxylic acid obtained in the above experiment was not good, at most about 35 per cent. of the theoretical yield. The lower boiling fractions and the solid substance mentioned above have not been further examined.

Acetoxytetramethylenecarboxylic Acid, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\ |\\ CH_2\cdot C(OC_2H_3O)\cdot COOH\end{matrix}$

In the course of experiments instituted with the object of eliminating the elements of water from hydroxytetramethylenecarboxylic acid, a

quantity of this acid was heated with sodium acetate and a large excess of acetic anhydride in a sealed tube at 200—230° for four hours.

The product was distilled until the greater bulk of the acetic anhydride had been removed, the residue cooled well, mixed with water, allowed to stand for some time, and extracted four times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a brownish oil; on fractionating this under reduced pressure, an almost colourless oil passed over, boiling at 200—220° (40 mm.), which on standing solidified almost entirely. The crystalline cake was spread on a porous plate to remove oily mother liquor, recrystallised from light petroleum, dried over sulphuric acid under reduced pressure, and analysed with the following result:—

I. 0·1495 gram substance gave 0·0880 gram H_2O and 0·2914 gram CO_2.

II. 0·1769 gram substance gave 0·1036 gram H_2O and 0·3447 gram CO_2.

	Theory. $C_7H_{10}O_4$.	Found. I.	Found. II.
C	53·17 per cent.	53·16	53·14 per cent.
H	6·33 „	6·54	6·50 „
O.....	40·50 „	40·30	40·36 „

This substance is acetoxytetramethylenecarboxylic acid. It crystallises from light petroleum (b. p. 68—70°) in groups of slender needles which melt at 72—74°. It is excessively soluble in benzene, alcohol, and ether, readily so in boiling light petroleum, but only sparingly in the latter in the cold. It dissolves readily in cold water, and is evidently very easily hydrolysed. The composition of this acid was further proved by hydrolysis with standard potassium hydrate solution (1 c.c. = 0·00559 gram KOH). 0·8316 gram of the acetate was dissolved in a little water, 150 c.c. of the potassium hydrate solution added, the mixture boiled for an hour in a reflux apparatus, and neutralised with standard sulphuric acid. It was thus found that 106·7 c.c. of the potassium hydrate solution had been neutralised during the hydrolysis; this corresponds to 0·5964 gram KOH, whereas the amount required to neutralise the hydroxytetramethylenecarboxylic acid and the acetic acid produced from the acetate would theoretically be 0·5893 gram KOH.

Ethoxytetramethylenecarboxylic Acid, $\begin{matrix} CH_2\cdot CH \\ | \quad\quad | \\ CH_2\cdot C(OC_2H_5)\cdot COOH. \end{matrix}$

If in the hydrolysis of monobromotetramethylenecarboxylic acid alcoholic instead of aqueous potash is employed, a substance is

obtained which boils constantly at 230—232° under the ordinary pressure; this, on analyis, gave numbers agreeing approximately with those required for ethoxytetramethylenecarboxylic acid, and it appeared to us interesting to determine whether by employing sodium ethylate instead of alcoholic potash, this ethoxy-acid might not be obtained in a pure state. 60 grams of methyl monobromotetramethylenecarboxylate was added to a solution of 16 grams of sodium in 200 grams of absolute alcohol, and the product boiled for two hours in a flask connected with a reflux apparatus. The solution, which contained a quantity of sodium bromide in suspension, was evaporated until the excess of alcohol had been removed, the residue dissolved in water, acidified with hydrochloric acid, and extracted 10 times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a slightly brownish oil which, on fractioning under reduced pressure (60 mm.), distilled for the most part between 160° and 175°. The colourless oil obtained on redistillation boiled at 164—165° (60 mm.), and, on analysis, gave the following numbers:—

I. 0·1996 gram substance gave 0·1500 gram H_2O and 0·4237 gram CO_2.

II. 0·1520 gram substance gave 0·1155 gram H_2O and 0·3240 gram CO_2.

	Theory. $C_7H_{12}O_3$.	Found. I.	Found. II.
C	58·33 per cent.	57·89	58·13 per cent.
H	8·33 „	8·35	8·44 „
O	33·33 „	33·76	33·43 „

Ethoxytetramethylenecarboxylic acid is a thick, colourless liquid which is readily soluble in water; it seems to be decomposed by boiling with aqueous potassium hydrate solution with formation of hydroxytetramethylenecarboxylic acid.

Tetramethylene Methyl Ketone, $\begin{matrix} CH_2{\cdot}CH_2 \\ | \quad\quad | \\ CH_2{\cdot}CH{\cdot}CO{\cdot}CH_3 \end{matrix}$.

This substance was readily prepared as follows:—15 grams of zinc methide was mixed with 50 grams of very carefully dried ether, 18 grams of pure tetramethylenecarboxylic chloride very slowly added, the temperature being kept below 30° by external cooling, and every precaution taken to exclude air and moisture as much as possible. At the end of about half an hour, water was cautiously added, the mixture allowed to stand for some time, the ethereal solution evaporated, and the residual almost colourless oil purified by distillation in a current of steam. The distillate was saturated with

potassium carbonate, extracted several times with ether, the ethereal solution evaporated, and the crude ketone purified in the following way :—

In order to remove traces of methyl tetramethylenecarboxylate, (produced by the action of $Zn(OCH_3)_2$ on the tetramethylenecarboxylic chloride, see p. 52), the oil was digested in alcoholic solution for 20 minutes with a small quantity of pure potassium hydrate, the ketone precipitated by the addition of water, extracted with ether, the ethereal solution well washed with water, dried over calcium chloride, evaporated, and the residual oil submitted to fractional distillation. In this way, about 11·6 grams of colourless oil was obtained boiling constantly at 134° (738 mm.).

The analysis gave the following results :—

I. 0·1024 gram substance gave 0·0977 gram H_2O and 0·2744 gram CO_2.

II. 0·1365 gram substance gave 0·1282 gram H_2O and 0·3670 gram CO_2.

	Theory. $C_6H_{10}O$.	Found. I.	Found. II.
C	73·47 per cent.	73·08	73·32 per cent.
H	10·20 „	10·60	10·43 „
O	16·33 „	16·32	16·25 „

Tetramethylene methyl ketone is a colourless mobile oil, sparingly soluble in water, and possessing a strong odour of peppermint; it combines with sodium hydrogen sulphite very readily, forming a beautifully crystalline, pearly double compound, which resembles acetone sodium hydrogen sulphite in appearance.

The density and magnetic rotation determinations gave the following results :—

Density.—$d\,4°/4° = 0·9160$; $d\,5°/5° = 0·9155$; $d\,10°/10° = 0·9106$; $d\,15°/15° = 0·9065$; $d\,20°/20° = 0·9028$; $d\,25°/25° = 0·8994$.

Magnetic Rotations.

	t.	Sp. rotation.	Mol. rotation.
	15·5°	0·9837	5·911
	15·5	0·9823	5·902
	15·5	0·9808	5·893
	16·5	0·9852	5·924
	16·5	0·9837	5·915
	19·7	0·9754	5·880
	19·7	0·9792	5·903
	19·7	0·9784	5·898
	19·7	0·9754	5·880
Average ..	17·6	0·9805	5·901

Comparing the magnetic rotation of tetramethylene methyl ketone with that of the nearest saturated ketone, that is, methyl butyl ketone, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3$, we find that the former possesses a rotation even smaller than the latter; thus:—

Methyl butyl ketone (calc.)	6·522
Less H_2 for difference in composition	0·508
	6·014
Tetramethylene methyl ketone	5·901
Difference	0·113

This shows at once that tetramethylene methyl ketone cannot be an unsaturated substance, because unsaturated substances invariably have much higher rotations than the corresponding saturated substances (compare W. H. Perkin, sen., Trans., 1889, **55**, 733—734). In a previous research on the products formed by the distillation of calcium tetramethylenecarboxylate with lime (Colman, Perkin, Trans., 1887, **51**, 237), a substance was obtained which boiled at 136—137°, and, on analysis, gave numbers agreeing with the formula $C_6H_{10}O$. It smelt strongly of peppermint, combined readily with sodium hydrogen sulphite, and in general possessed properties which led the authors to the conclusion that it was tetramethylene methyl ketone. There can be doubt that this substance is identical with the product obtained by the action of tetramethylenecarboxylic chloride on zinc methide.

Tetramethylene methyl ketone is isomeric with methyldehydrohexone, $\begin{matrix} CH_3{\cdot}C & -O- & CH_2 \\ \| & & | \\ CH{\cdot}CH_2{\cdot}CH_2 & & \end{matrix}$, which was obtained by the distillation of methyldehydrohexonecarboxylic acid (Trans., 1887, **51**, 723).

Tetramethylene Methyl Ketoxime, $\begin{matrix} CH_2{\cdot}CH_2 \\ | \quad | \\ CH_2{\cdot}CH{\cdot}C(:NOH){\cdot}CH_3 \end{matrix}$.

In order to obtain this substance, 5 grams of the pure ketone was dissolved in methyl alcohol, mixed with a solution of 13 grams of pure potassium hydrate in methyl alcohol, a concentrated aqueous solution of 5·3 grams of hydroxylamine hydrochloride added, and the whole allowed to stand for 15 hours. The product was mixed with water, the solution rendered slightly acid by the addition of hydrochloric acid, and extracted three times with ether; the ethereal solution was then washed with water, dried over calcium chloride, and the residual oily oxime purified by distillation under the ordinary pressure. Almost the whole distilled between 194° and 195° as a colourless oil, which solidified completely on standing for some days. The crystals

were freed from traces of oily mother liquor by spreading on a porous plate, recrystallised from water, and the thick, colourless prisms thus obtained, after drying over sulphuric acid under reduced pressure, analysed with the following results :—

0·1166 gram substance gave 0·1064 gram H_2O and 0·2274 gram CO_2.
0·1309 gram substance gave 13·7 c.c. N ; $t = 13°$; bar. = 755 mm.

	Theory. $C_6H_{11}NO$.	Found.
C	63·72 per cent.	63·71 per cent.
H.....	9·73 „	10·14 „
N	12·39 „	12·25 „

Tetramethylene methyl ketoxime melts at 60—61°, and possesses in a marked degree the odour characteristic of oximes. It is readily soluble in alcohol, benzene, light petroleum, and hot water, less so in cold water; it dissolves readily in concentrated hydrochloric acid, and in moderately concentrated sodium hydrate solution in the cold. If the solution in hot water is allowed to cool slowly, the ketoxime is gradually deposited in beautiful, colourless, six-sided prisms.

Tetramethylenemethylcarbinol, $\begin{matrix} CH_2{\cdot}CH_2 \\ | \quad\quad | \\ CH_2{\cdot}CH{\cdot}CH(OH){\cdot}CH_3 \end{matrix}$.

The reduction of tetramethylene methyl ketone to the corresponding secondary alcohol is readily accomplished by means of sodium in moist ethereal solution. 10 grams of the pure ketone was dissolved in 100 grams of pure ether; the solution floated on a strong solution of sodium hydrate, contained in a stout bottle fitted with a reflux condenser, and then a large excess of sodium gradually added, and small quantities of water from time to time, if necessary, the course of the reaction being moderated by cooling the bottle with a stream of water. The ethereal solution was separated, washed with a little very dilute hydrochloric acid, then with water, dried over potassium carbonate, evaporated, and the oily residue purified by fractional distillation. Almost the whole passed over between 140° and 150°, leaving only a very small residue of high boiling point in the retort; on redistillation, a colourless oil was obtained boiling constantly at 144—145° ; this gave the following results on analysis :—

0·1942 gram substance gave 0·2142 gram H_2O and 0·5071 gram CO_2.

	Theory. $C_6H_{12}O$.	Found.
C	72·00 per cent.	71·78 per cent.
H	12·00 „	12·25 „
O	16·00 „	15·97 „

Tetramethylenemethylcarbinol is a colourless, mobile liquid, possessing a powerful odour strongly resembling that of menthol; it boils constantly at 144—145°.

Tetramethylene Ethyl Ketone, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CO\cdot C_2H_5\end{matrix}$.

This ketone is readily produced by the action of tetramethylenecarboxylic chloride on zinc ethide, and as considerable quantities of it were required, numerous experiments were instituted with the object of working out a method of preparation which would give a good yield of the pure substance. Ultimately the following process was adopted:—

Into a large flask, filled with dry carbonic anhydride, about 100 grams of very carefully purified and thoroughly dry ether is placed; 30 grams of zinc ethide are added, and then 50 grams of tetramethylenecarboxylic chloride slowly dropped in from a dropping funnel. At first, scarcely any reaction appears to take place, and there is very little evolution of heat, but, on standing for a few minutes, the mixture rapidly becomes warm, and a very vigorous reaction sets in, so that it is necessary to watch, and now and then cool the flask under the tap, otherwise loss from boiling over may occur. As soon as the decomposition is at an end, water is cautiously added, the ethereal solution separated, evaporated, and the residual oil submitted to distillation in a current of steam. The distillate is extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the crude ketone fractionated.

In our first experiments, almost the whole of the ketone thus prepared boiled constantly at 153°, and gave the following results on analysis:—

I. 0·2036 gram substance gave 0·1860 gram H_2O and 0·5300 gram CO_2.

II. 0·1026 gram substance gave 0·0954 gram H_2O and 0·2672 gram CO_2.

	Theory. $C_7H_{14}O$.	Found. I.	Found. II.
C	75·00 per cent.	70·99	71·02 per cent.
H	10·72 „	10·14	10·33 „
O	14·28 „	18·87	18·65 „

These analyses differ from theory by a minus of 4 per cent. of carbon and 0·5 per cent. of hydrogen, and for a long time no explanation of this curious discrepancy was forthcoming.

Ultimately it was discovered that the liquid was a a mixture con-

taining considerable quantities of ethyl tetramethylenecarboxylate, the formation of which must be due to the action of tetramethylenecarboxylic chloride on zinc ethylate contained in the zinc ethide employed, thus:—

$$2\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot COCl\end{matrix} + Zn(OC_2H_5)_2 = 2\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot COOC_2H_5\end{matrix} + ZnCl_2,$$

and as this ethereal salt boils at approximately the same temperature as the ketone, a separation by fractional distillation was out of the question. In order to obtain the pure ketone from this mixture, the oil was digested with an excess of alcoholic potash for one hour in a flask connected with a reflux apparatus, the product mixed with water, distilled with steam, the distillate extracted with pure ether, the ethereal solution dried over calcium chloride, evaporated, and the colourless, oily residue purified by fractionation.

During the first distillation, almost the whole passed over between 154° and 157°, leaving only a very small residue in the retort, and on repeated fractionation, a colourless oil was obtained boiling constantly at 155—156°; this, on analysis, gave the following results:—

0·1529 gram substance gave 0·1528 gram H_2O and 0·4199 gram CO_2.

	Theory. $C_7H_{12}O$.	Found.
C	75·00 per cent.	74·89 per cent.
H	10·72 „	11·10 „
O	14·28 „	14·01 „

Tetramethylene ethyl ketone is a colourless, mobile oil, smelling strongly of peppermint. It boils at 155—156°, and is less soluble in water than the corresponding methyl ketone.

A vapour density determination of this substance, made by Hofmann's method in a vacuum, at the temperature of boiling aniline, gave—

		Theory. $C_7H_{14}O$.	
D.....	3·6	D.....	3·8

The density and magnetic rotation determinations of tetramethylene ethyl ketone gave the following results:—

Density.—d 4°/4° = 0·9094; d 5°/5° = 0·9086; d 10/°10° = 0·9044; d 15°/15° = 0·9004; d 20°/20° = 0·8970; d 25°/25° = 0·8934.

Magnetic Rotations.

	t.	Sp. rotation.	Mol. rotation.
	17·0°	1·0052	6·963
	17·0	0·9990	6·922
	17·0	1·0012	6·936
	19·0	0·9988	6·923
	19·0	0·9988	6·923
	19·0	0·9921	6·877
	19·0	0·9861	6·836
Average ..	18·1	0·9972	6·911

As in the case of tetramethylene methyl ketone, this ketone has a rotation *lower* than the nearest corresponding saturated ketone which has been examined (butyrone). Thus—

Magnetic rotation of butyrone	7·489
Less H_2 for difference in composition	0·508
	6·981
Tetramethylene ethyl ketone	6·911
Difference	0·070

Sodium Hydrogen Sulphite Compound of Tetramethylene Ethyl Ketone, $C_7H_{14}O,NaHSO_3$.

When shaken with a concentrated solution of sodium hydrogen sulphite containing a large excess of sulphurous anhydride, tetramethylene ethyl ketone gradually dissolved, and the solution, on standing, slowly deposited beautiful, glistening prisms. These were collected, washed with water, dried first on a porous plate and then over sulphuric acid, and analysed with the following result :—

0·1498 gram substance, heated with sulphuric acid, gave 0·0518 gram Na_2SO_4.

	Theory. $C_7H_{12}O,NaHSO_3$.	Found.
Na	10·65 per cent.	11·18 per cent.

This substance is moderately soluble in water; when warmed with dilute sulphuric acid, or with sodium carbonate solution, it is decomposed, with separation of an oil, which is obviously the regenerated ketone. Grimm (*Annalen*, **157**, 262) states that only methyl ketones combine with sodium hydrogen sulphite. Tetramethylene ethyl ketone is an exception to this rule.

Tetramethylene Ethyl Ketoxime, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\ \ |\\ CH_2\cdot CH\cdot C(:NOH)\cdot C_2H_5\end{matrix}$.

In preparing this oxime, 7 grams of the pure ketone was dissolved in a solution of 15 grams of pure potassium hydrate in methyl alcohol, 6 grams of hydroxylamine hydrochloride dissolved in the smallest possible quantity of water added, and the whole allowed to stand for 15 hours. The product was mixed with water, rendered slightly acid by the addition of hydrochloric acid, extracted three times with ether, the ethereal solution washed with water, dried over calcium chloride, evaporated, and the residual oil purified by fractionation.

Tetramethylene ethyl ketoxime is a thick, colourless oil boiling constantly at 208—209° (750 mm.); it does not solidify even on long standing. It dissolves easily in hydrochloric acid, and, on warming, the solution is rapidly decomposed with regeneration of the ketone.

A carefully purified sample of this oxime gave the following results on analysis :—

0·1248 gram substance gave 0·1178 gram H_2O and 0·3011 gram CO_2.

0·1369 gram substance gave 13·3 c.c. N; t = 15·5°; bar. = 748 mm.

	Theory. $C_7H_{13}NO$.	Found.
C	66·14 per cent.	65·97 per cent.
H	10·24 „	10·48 „
N	11·02 „	11·15 „

Tetramethyleneethylcarbinol, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\ \ |\\ CH_2\cdot CH\cdot CH(OH)\cdot C_2H_5\end{matrix}$.

In order to prepare this secondary alcohol, we experimented in the first place on the action of sodium amalgam on the dilute alcoholic solution of tetramethylene ethyl ketone; 29 grams of the pure ketone was dissolved in 80 grams of alcohol, water was then added until a very faint turbidity was produced, and the solution treated with 1200 grams of 2½ per cent. sodium amalgam, in quantities of about 200 grams at a time, the ketone being kept in solution, and the reaction promoted by the occasional addition of dilute alcohol. As soon as the amalgam had been completely decomposed, the whole was mixed with water, the mercury run off, and the solution extracted several times with ether. After washing with water, drying over potassium carbonate, and evaporating the ethereal solution, a colourless oil was left which boiled constantly at 155—156°, and, on analysis, gave numbers agreeing with the formula $C_7H_{12}O$, showing that no

reduction had taken place, and in fact almost the whole of the ketone was recovered unchanged.

After this curious result, no further experiments were made on the action of sodium amalgam on tetramethylene ethyl ketone, as it was found that it could be reduced to the carbinol with great ease by means of sodium in moist ethereal solution.

24 grams of the pure ketone was dissolved in about 300 c.c. of pure ether, the ethereal solution floated on water, and treated with a large excess of sodium, the operation being conducted exactly as described under tetramethylenemethylcarbinol (p. 50). During the reduction, a considerable quantity of a white sodium compound separated, which was probably the sodium compound of the carbinol; this was readily decomposed by the addition of water. As soon as the last traces of the sodium had disappeared, the ethereal solution was separated, washed with very dilute hydrochloric acid, dried over anhydrous potassium carbonate, evaporated, and the almost colourless residue distilled under reduced pressure. Almost the whole of it passed over at 120° (290 mm.), leaving only a very slight residue in the retort, and this fraction, on subsequent distillation under ordinary pressures, boiled constantly at 162° (754 mm.); the yield obtained was fully 20 grams.

The substance was once more fractioned, and then analysed with the following result:—

0·1183 gram substance gave 0·1320 gram H_2O and 0·3189 gram CO_2.

	Theory. $C_7H_{14}O$.	Found.
C.....	73·68 per cent.	73·52 per cent.
H.....	12·27 „	12·39 „
O.....	14·05 „	14·09 „

Tetramethyleneethylcarbinol is a colourless oil of agreeable odour, sparingly soluble in water. It boils constantly at 162°. The density and magnetic rotation determinations gave the following results:—

Density.—d 4°/4° = 0·9092; d 5°/5° = 0·9083; d 10°/10° = 0·9044; d 15°/15° = 0·9007; d 20°/20° = 0·8974; d 25°/25° = 0·8945.

Magnetic Rotations.

t.	Sp. rotation.	Mol. rotation.
18·4°	1·0384	7·319
18·4	1·0445	7·368
18·4	1·0394	7·327
18·4	1·0363	7·303
19·0	1·0347	7·297
19·0	1·0371	7·317
19·0	1·0378	7·321
19·0	1·0378	7·321
20·0	1·0386	7·329
20·0	1·0377	7·322
20·0	1·0407	7·346
Average 18·8	1·0384	7·325

On examining these numbers, it will be seen that the relation between tetramethylene ethyl ketone and tetramethyleneethylcarbinol is very similar to that between a ketone and a secondary alcohol in the fatty series, thus :—

Magnetic rotation of isopropyl alcohol	4·019
,, ,, acetone	3·514
Difference	0·505
Magnetic rotation of tetramethyleneethylcarbinol...	7·325
,, ,, tetramethylene ethyl ketone ..	6·911
Difference	0·414

Tetramethyleneethylcarbinyl Acetate, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CH(OC_2H_3O)\cdot C_2H_5\end{matrix}$.

In order to prepare this acetate, 5 grams of the pure carbinol was digested with 15 grams of acetic anhydride for 15 minutes, the product distilled, and then very carefully fractionated, in order to separate the acetate as completely as possible from unchanged acetic anhydride. After four fractionations, a colourless oil was obtained which boiled constantly at 178—179°, and gave the following results on analysis :—

0·1158 gram substance gave 0·1071 gram H_2O and 0·2912 gram CO_2.

	Theory. $C_9H_{16}O_2$.	Found.
C	69·23 per cent.	68·58 per cent.
H	10·26 ,,	10·27 ,,
O	20·51 ,,	21·15 ,,

Tetramethyleneethylcarbinyl acetate is a colourless oil possessing the odour characteristic of the acetates of the higher alcohols of the fatty series; it is readily hydrolysed by boiling with aqueous potassium hydrate solution. A quantitative experiment was made in order to determine the amount of acetic acid produced by the hydrolysis.

1·2511 grams of the substance was boiled in a reflux apparatus with 150 c.c. of standard potassium hydrate solution for six hours, allowed to cool, and the solution neutralised by the addition of standard sulphuric acid solution.

83·1 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH) had been neutralised during the hydrolysis; this corresponds to 39·65 per cent. acetic acid, whereas $C_9H_{16}O_2$ should yield on hydrolysis 38·46 per cent. acetic acid.

This result shows that, in spite of careful fractionation, the acetate probably still contained traces of acetic anhydride; this would account for the slight deficiency of carbon found in the elementary analysis.

Tetramethylenepropyl Iodide, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CHI\cdot C_2H_5\end{matrix}$, *and Tetramethylenepropyl Bromide*, $C_7H_{13}Br$.

Tetramethyleneethylcarbinol readily reacts with hydriodic acid with formation of tetramethylenepropyl iodide, thus:—

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CH(OH)\cdot C_2H_5\end{matrix} + HI = \begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CHI\cdot C_2H_5\end{matrix} + H_2O.$$

7·5 grams of the pure carbinol was shaken with 40 grams of fuming hydriodic acid (sp. gr. 1·96); the mixture, which became very warm, allowed to stand over night, and then heated to boiling in a flask connected with a reflux apparatus for a few minutes. The product was poured into water, extracted twice with ether, the ethereal solution washed well with water containing a little sulphurous anhydride, dried over calcium chloride, evaporated, and the slightly brownish, oily residue purified by fractionation under reduced pressure. In this way, a colourless oil was obtained which boiled constantly at 105—107° (80 mm.), and gave the following results on analysis:—

0·2915 gram substance gave 0·2998 gram AgI.

	Theory. $C_7H_{13}I$.	Found.
I.....	56·69 per cent.	55·62 per cent.

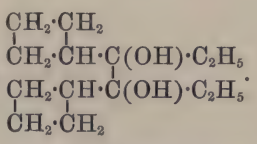
Tetramethylenepropyl iodide is a heavy, colourless oil, which possesses an odour strongly resembling that of hexyl iodide. When pure, it may be distilled in small quantities under ordinary pressures with only slight decomposition, but the crude substance cannot be purified by fractionation except under greatly reduced pressure, and even then slight decomposition seems to take place, as indicated by the above analysis. The pure iodide soon turns brown on exposure to light. It is rapidly decomposed by boiling with water with formation of hydriodic acid. When heated in a sealed tube with fuming hydriodic acid and amorphous phosphorus at 230°, it is readily reduced with formation of a hydrocarbon, which is at present under investigation.

Tetramethylenepropyl bromide, $C_7H_{13}Br$, is similarly produced by the action of hydrobromic acid (sp. gr. 1·83) on tetramethyleneethylcarbinol. It is a colourless oil, which has an odour closely resembling that of trimethylene bromide; it boils constantly at 110° (120 mm.). Analysis:—

0·2336 gram substance gave 0·2430 gram AgBr.

	Theory. $C_7H_{13}Br$.	Found.
Br.....	45·20 per cent.	44·51 per cent.

Ditetramethylene Diethyl Glycol,



Two experiments on the reduction of tetramethylene ethyl ketone in moist ethereal solution by means of sodium were made; in the first, an almost quantitative yield of tetramethyleneethylcarbinol was obtained; whilst in the second, conducted apparently under precisely similar conditions, a comparatively small quantity of the carbinol was produced, and the product, on distillation under reduced pressure, gave a considerable fraction boiling at 220—223° (100 mm.), which, on standing, almost completely solidified. The crystals were spread on a porous plate until free from oily mother liquor, dried over sulphuric acid, and analysed (I). The substance was then purified by recrystallisation from light petroleum and again analysed (II).

I. 0·1392 gram substance gave 0·1447 gram H_2O and 0·3790 gram CO_2.

II. 0·1525 gram substance gave 0·1596 gram H_2O and 0·4155 gram CO_2.

	Theory. $C_{14}H_{26}O_2$.	Found. I.	Found. II.
C	74·34 per cent.	74·26	74·31 per cent.
H	11·50 „	11·55	11·41 „
O	14·16 „	14·19	14·28 „

The molecular weight was determined by Raoult's method, using acetic acid as the solvent, with the following results:—

Weight of substance taken	0·4643 gram.
Weight of acetic acid taken	24·35 grams.
Melting point of the acetic acid	16·19°
„ „ mixture.....	15·87°
Depression of the melting point.....	0·32°
Molecular weight, $C_{14}H_{26}O_2$	226
Found	232

This substance is, therefore, ditetramethylene diethyl glycol, the pinacone derived from tetramethylene ethyl ketone.

It melts at 95°, and, when liquid, smells strongly of peppermint; it is very readily soluble in alcohol, benzene, and warm light petroleum, sparingly in water; on slowly cooling its solution in warm light petroleum, it crystallises in curiously striated masses consisting of transparent, colourless prisms usually radiating from a centre.

Tetramethylene Phenyl Ketone, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot CO\cdot C_6H_5\end{matrix}$.

This interesting compound is produced when a solution of tetramethylenecarboxylic chloride in excess of benzene is treated with aluminium chloride:

$$\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot COCl\end{matrix} + C_6H_6 = \begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH_2\cdot CH\cdot CO\cdot C_6H_5\end{matrix} + HCl.$$

The following method, which has been repeatedly employed, gives a good yield of tetramethylene phenyl ketone:—

40 grams of pure aluminium chloride and 100 grams of pure, dry benzene (free from thiophen) are mixed in a large flask, and then a solution of 30 grams of tetramethylenecarboxylic chloride in 60 grams of benzene slowly added through a dropping funnel. During the operation, the mixture becomes slightly warm, and some hydrogen chloride is evolved; the product, after standing for 15 minutes, is heated to boiling in a reflux apparatus by means of a water-bath for half an hour, well cooled, and gradually mixed with

water containing some hydrochloric acid. The upper benzene layer is separated, washed with water containing a little sodium carbonate, dried over calcium chloride, the benzene distilled off, and the residual crude, dark-coloured ketone distilled under reduced pressure. About 22 grams of a colourless oil boiling at 180—200° (150 mm.) are obtained, and this, on fractionation under ordinary pressures, distils almost entirely between 258° and 259° (740 mm.).

The analysis of this substance gave the following numbers :—

0·1280 gram substance gave 0·0874 gram H_2O and 0·3859 gram CO_2.

	Theory. $C_{11}H_{12}O$.	Found.
C	82·50 per cent.	82·22 per cent.
H	7·50 ,,	7·59 ,,
O	10·00 ,,	10·21 ,,

The molecular weight was determined by Raoult's method, using acetic acid as the solvent, with the following results :—

Weight of substance taken	0·9368 gram
,, acetic acid taken	50·85 grams
Melting point of the acetic acid.....	15·009°
,, ,, mixture.....	14·590°
Depression of the melting point.....	0·419°
Molecular weight, $C_{11}H_{12}O$	160
Found.....	170

Tetramethylene phenyl ketone is a thick, colourless oil which boils without decomposition at 258—259°, but, on standing, soon acquires a slight yellowish tinge; it has an odour which can scarcely be distinguished from that of butyl phenyl ketone,

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_3$$

(b. p. 236—238° at 720 mm.). It is isomeric with phenyldehydrohexone, $C_6H_5\cdot C(O\cdot CH_2\cdot CH_2)\cdot CH\cdot CH_2$, which boils at 249—251° (Trans., 1887, **51**, 731).

The density and magnetic rotation determinations of this substance gave the following results :—

Density.—$d\,4°/4° = 1·0600$; $d\,5°/5° = 1·0591$; $d\,10°/10° = 1·0551$; $d\,15°/15° = 1·0515$; $d\,20°/20° = 1·0485$; $d\,25°/25° = 1·0457$.

Magnetic Rotation.

t.	Sp. rotation.	Mol. rotation.
16·5°	1·8234	15·431
16·5	1·8300	15·485
16·5	1·8345	15·523
16·5	1·8330	15·510
18·5	1·8260	15·469
18·5	1·8266	15·474
18·5	1·8314	15·515
18·5	1·8230	15·443
19·5	1·8160	15·391
19·5	1·8136	15·371
19·5	1·8226	15·448
Average 18·0	1·8255	15·460

The magnetic rotation of tetramethylene phenyl ketone may be calculated from that of the corresponding ethyl ketone, thus:—

Magnetic rotation of tetramethylene ethyl ketone..	6·911
— the value of C_2H_4	2·046
	4·865
+ the value of C_6H_5 replacing hydrogen....	10·406
Calculated magnetic rotation of tetramethylene phenyl ketone	15·271
This number agrees well with that actually found, namely	15·460

Tetramethylene Phenyl Ketoxime, $\begin{matrix}CH_2\cdot CH_2\\ |\quad\quad |\\ CH_2\cdot CH\cdot C(:NOH)\cdot C_6H_5\end{matrix}$.

In order to prepare this substance, 5 grams of the pure ketone was dissolved in methyl alcohol, mixed with a solution of 8 grams of potassium hydrate dissolved in methyl alcohol, a concentrated aqueous solution of 3·3 grams of hydroxylamine hydrochloride added, and the mixture allowed to stand for 15 hours. On diluting the product with water, the oxime separated in colourless needles; these were extracted with ether, the ethereal solution washed with water, dried over calcium chloride, evaporated, and the solid residue purified by recrystallisation from 80 per cent. alcohol. The beautiful, colourless needles thus obtained, after drying over sulphuric acid under reduced pressure, gave the following numbers on analysis:—

0·1207 gram substance gave 0·0832 gram H_2O and 0·3322 gram CO_2.

0·1944 gram substance gave 12·9 c.c. N; $t = 9·5°$; bar. = 758 mm.

	Theory. $C_{11}H_{13}NO$.	Found.
C.....	75·42 per cent.	75·10 per cent.
H.....	7·42 „	7·66 „
N.....	8·00 „	7·93 „

Tetramethylene phenyl ketoxime melts at 91—93°. It is readily soluble in benzene and alcohol, but only sparingly in cold light petroleum, and almost insoluble in water. It dissolves readily in strong hydrochloric acid in the cold, and in warm, dilute potassium hydrate solution. It crystallises from dilute alcohol in colourless needles, and from light petroleum in long, thin, slender needles.

The oxime dissolves very readily in acetyl chloride with slight evolution of heat; on distilling off the acetyl chloride and heating the residue, a very violent reaction sets in, the original colourless liquid becoming quite brown. If the semi-solid residue is distilled with concentrated potassium hydrate solution, a strong odour of aniline is noticeable, and it appears probable that in the above reaction the oxime undergoes intramolecular change, with formation of the anilide of tetramethylenecarboxylic acid, $\begin{matrix}CH_2{\cdot}CH_2\\ |\quad\ \ |\\ CH_2{\cdot}CH{\cdot}CO{\cdot}NH{\cdot}C_6H_5\end{matrix}$ This point is being further investigated.

Reduction of Tetramethylene Phenyl Ketone. Formation of Tetramethylenephenylcarbinol, $\begin{matrix}CH_2{\cdot}CH_2\\ |\quad\ \ |\\ CH_2{\cdot}CH{\cdot}CH(OH){\cdot}C_6H_5.\end{matrix}$

This reduction was conducted exactly as in the case of the reduction of the corresponding ethyl and methyl ketones. 36 grams of tetramethylene phenyl ketone was dissolved in ether, the solution floated on water, and treated with 40 grams of sodium; the ethereal solution was then washed with water containing a little hydrochloric acid, allowed to stand for about 24 hours, until no more crystals of ditetramethylene diphenyl glycol separated (p. 66), filtered, dried over potassium carbonate, evaporated, and the residual oil purified by fractionation under reduced pressure. In this way a colourless oil (21 grams) was obtained boiling constantly at 180° (100 mm.), but there was a considerable residue in the retort, which will be referred to later on. The analysis of the substance boiling at 180° (100 mm.) gave the following results:—

I. 0·1679 gram substance gave 0·1412 gram H_2O and 0·4979 gram CO_2.

II. 0·1409 gram substance gave 0·1188 gram H_2O and 0·4188 gram CO_2.

	Theory. $C_{11}H_{14}O$.	Found. I.	Found. II.
C	81·48 per cent.	80·87	81·06 per cent.
H	8·64 „	9·34	9·36 „
O	9·88 „	9·79	9·58 „

The product was then refractioned at ordinary pressures, when, almost the whole passed over at 257° (752 mm.), and, on analysis, gave the following results:—

I. 0·1111 gram substance gave 0·0942 gram H_2O and 0·3299 gram CO_2.

II. 0·1734 gram substance gave 0·1436 gram H_2O and 0·5123 gram CO_2.

	Found. I.	Found. II.
C.....	80·98	80·57 per cent.
H	9·42	9·20 „
O.....	9·60	9·23 „

The refractionation had not materially altered the composition of the substance. It will be seen that this alcohol contains considerably more hydrogen than is required by the formula $C_{11}H_{14}O$, and this very curious result can only be explained on the assumption that during the reduction the benzene ring has been partially reduced. This is borne out by the results obtained in the determination of the magnetic rotation of this preparation.

Density.—$d\,4°/4° = 1·0309$; $d\,5°/5° = 1·0301$; $d\,10°/10° = 1·0265$; $d\,15°/15° = 1·0231$; $d\,20°/20° = 1·0201$; $d\,25°/25° = 1·0175$.

Magnetic Rotations.

t.	Sp. rotation.	Mol. rotation.
14·0°	1·7043	14·982
14·0	1·6932	14·884
14·0	1·6979	14·926
14·0	1·6964	14·913
16·37°	1·6848	14·833
16·37	1·6926	14·901
16·37	1·6915	14·892
16·37	1·6859	14·842
16·37	1·6903	14·881
Average 15·31	1·6930	14·895

The effect of reducing tetramethylene ethyl ketone to the corresponding carbinol is to raise the magnetic rotation by 0·414; and as the reduction of tetramethylene phenyl ketone proceeds on exactly the same lines, the magnetic rotation of tetramethylenephenylcarbinol may be calculated thus:—

Magnetic rotation of tetramethylene phenyl ketone	15·460
+ the effect produced by adding H_2 to the carbonyl group	0·414
Calculated rotation of tetramethylenephenylcarbinol	15·874
Result obtained in the above experiments	14·895
Deficiency	0·979

As benzene has an abnormally high rotation, the saturated hydrocarbons, on the other hand, a low rotation, the above deficiency may be easily accounted for on the assumption that the substance contains a compound in which the benzene ring has been partially reduced. Experiments on the action of sodium in moist ethereal solution on other benzene derivatives, such as acetophenone, have given results which clearly indicate that in these cases also the benzene ring is partially reduced, although the derivatives obtained have not yet been obtained in a pure condition (compare also Perkin and Schloesser, Trans., 1890, **57**, 955).

In order to obtain pure tetramethylenephenylcarbinol, the experiments on the reduction of the ketone in moist ethereal solution were repeated on a smaller scale, twice the quantity of sodium (for H_2) being employed. In this way a colourless oil was obtained which distilled at 257—259° (750 mm.), and gave the following results on analysis:—

0·1550 gram substance gave 0·1240 gram H_2O and 0·4621 gram CO_2.

	Theory. $C_{11}H_{14}O$.	Found.
C	81·48 per cent.	81·31 per cent.
H	8·64 „	8·89 „
O	9·88 „	9·80 „

Tetramethylenephenylcarbinol is a thick, colourless oil, possessing an odour closely resembling that of phenylmethylcarbinol, although not quite so pronounced. It is sparingly soluble in water; it does not dissolve in, but it reacts readily with, concentrated aqueous solutions of hydrobromic and hydriodic acids, forming heavy oils, which are probably the corresponding bromide and iodide of benzyltetramethylene.

Polymeride of Tetramethylenephenylcarbinol.—In fractioning the crude product of the reduction of tetramethylene phenyl ketone, a thick, yellow substance boiling above 190° (100 mm.) was always left in the flask. The small quantities obtained from several operations were collected and rapidly distilled from a small fractionating flask under a pressure of 60 mm., and the thick oil which boiled almost constantly at 320° analysed with the following result:—

0·1062 gram substance gave 0·0882 gram H_2O and 0·3159 gram CO_2.

	Theory. $C_{22}H_{28}O_2$.	Found.
C	81·48 per cent.	81·12 per cent.
H	8·64 „	9·22 „
O	9·88 „	9·66 „

The determination of the molecular weight by Raoult's method, using acetic acid as the solvent, gave the following results:—

Weight of substance taken.....	1·2644 grams.
Weight of acetic acid taken.....	31·68 grams.
Melting point of the acetic acid.....	16·14°
Melting point of the mixture.....	15·625°
Depression of the melting point.....	0·515°
Molecular weight, $C_{22}H_{28}O_2$.....	322
Found	302

This substance has, therefore, the formula $C_{22}H_{28}O_2$, and must be looked upon as a polymeride of tetramethylenephenylcarbinol containing 2 mols. of this carbinol, thus:—

$$C_{22}H_{28}O_2 = 2C_{11}H_{14}O.$$

When it is slowly distilled under a pressure of 100 mm., it is gradually decomposed, and on repeating the operation several times, a large quantity of an oil of comparatively low boiling point is obtained; this, on fractionation under ordinary pressures, boils constantly at 256—257°, and consists of pure tetramethylenephenylcarbinol, as the following analysis shows:—

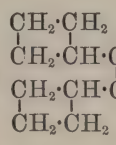
0·1150 gram substance gave 0·0879 gram H_2O and 0·3440 gram CO_2.

	Theory. $C_{11}H_{14}O$.	Found.
C.....	81·48 per cent.	81·40 per cent.
H.....	8·64 „	8·47 „
O.....	9·88 „	10·13 „

If the distillation is repeated sufficiently often, it appears that the

whole of this polymeride may in this way be converted into pure tetramethylenephenylcarbinol.

Ditetramethylene Diphenyl Glycol,



When the ethereal solution of the reduction products of tetramethylenephenylcarbinol (see preceding section) was allowed to stand for about 24 hours, a white, crystalline substance separated; this was collected, well washed with ether, recrystallised from this solvent, and analysed with the following results:—

I. 0·1390 gram substance gave 0·1026 gram H_2O and 0·4180 gram CO_2.

II. 0·1740 gram substance gave 0·1282 gram H_2O and 0·5225 gram CO_2.

III. 0·1884 gram substance gave 0·1398 gram H_2O and 0·5613 gram CO_2.

	Theory. $C_{22}H_{26}O_2$.	Found. I.	II.	III.
C	81·98 per cent.	82·04	81·90	81·29 per cent.
H	8·08 „	8·20	8·18	8·24 „
O	9·94 „	9·76	9·92	10·47 „

The molecular weight was determined by Raoult's method, using acetic acid as the solvent, with the following results:—

Weight of substance taken	0·5839 gram.
Weight of acetic acid taken.....	28·5 grams.
Melting point of the acetic acid..	16·19°
„ „ mixture	15·95°
Depression of the melting point ..	0·24°
Molecular weight, $C_{22}H_{26}O_2$.....	322
Found	333

This substance has therefore the formula $C_{22}H_{26}O_2$, and is obviously the pinacone of tetramethylene phenyl ketone.

Ditetramethylene diphenyl glycol melts at 153—154°. It dissolves readily in boiling glacial acetic acid and toluene, moderately easily in boiling alcohol, but only sparingly in ether and light petroleum. On slowly cooling its solution in boiling glacial acetic acid, it crystallises in long, colourless needles grouped together in parallel bundles.

LONDON:
HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY,
ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, July*, 1889. Vol. LV.]

$\alpha\omega$-DIACETYLPENTANE AND $\alpha\omega$-DIBENZOYLPENTANE.

By F. Stanley Kipping, Ph.D., D.Sc., and W. H. Perkin, Jun., Ph.D.

Under the influence of dehydrating agents, acetone readily undergoes condensation with formation of mesityl oxide, phorone, and other substances. The reaction in the case of mesityl oxide is represented by the equation—

$$\begin{matrix} CH_3\cdot CO\cdot CH_3 \\ CH_3\cdot CO\cdot CH_3 \end{matrix} = \begin{matrix} CH_3\cdot CO\cdot C \\ \| \\ CH_3\cdot C\cdot CH_3 \end{matrix} + H_2O.$$

Furthermore, when acetone is treated with certain reducing agents it yields pinacone, thus:—

$$\begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CO + CO\!<\!\begin{matrix} CH_3 \\ CH_3 \end{matrix} + H_2 = \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!C(OH)\cdot C(OH)\!<\!\begin{matrix} CH_3 \\ CH_3 \end{matrix}.$$

In each of these reactions, 2 mols. of acetone take part, the resulting compounds being formed by the direct union of two carbon-atoms, one from each molecule.

In studying these curious reactions, it seemed possible that, starting with diketones of the formula $R\cdot CO\cdot CH_2\cdot[CH_2]_n\cdot CH_2\cdot CO\cdot R$, and subjecting them to similar treatment, the condensation might be confined to one molecule.

Thus, under the influence of dehydrating agents, the change would be—

$$R\cdot CO\cdot CH_2\cdot[CH_2]_n\cdot CH_2\cdot CO\cdot R - H_2O = R\cdot C \begin{matrix} \diagdown \\ \diagup \end{matrix} \!\!\!\

short account of several less important substances which have been obtained in the course of this investigation.

Preparation of Ethyl Methyldehydrohexonecarboxylate and Acetobutyl Bromide.

In previous researches in which ethyl methyldehydrohexonecarboxylate has been employed, this substance was always prepared by treating 2 mols. of ethyl acetoacetate with 2 mols. of sodium ethylate and 1 mol. of trimethylene bromide, thus:—

$$2CH_3\cdot CO\cdot CHNa\cdot COOC_2H_5 + C_3H_6Br_2 =$$

$$\begin{matrix} CH_3\cdot C & \!\!=\!\!=\!\!= & C\cdot COOC_2H_5 \\ O< & & >CH_2 \\ & CH_2\cdot CH_2 & \end{matrix} + CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5 + 2NaBr.$$

The objection to this method is, that one-half of the ethyl acetoacetate is regenerated, and this on subsequent fractionating can be separated only very partially from the ethyl methyldehydrohexonecarboxylate, and is thus practically wasted.

As it was necessary for us to employ large quantities of this substance, we have made a number of experiments with a view to improve the method of preparation. As the result of these we find the following process to give the best results:—

130 grams of ethyl acetoacetate are added in small quantities at a time to a cold solution of 23 grams of sodium in 250 grams of absolute alcohol, care being taken that the temperature of the mixture does not rise above 40°; 202—205 grams of trimethylene bromide are now added, and the whole heated to boiling in a water-bath, in a flask connected with a reflux apparatus. As soon as the solution begins to boil, the separation of sodium bromide commences and a vigorous reaction sets in, the heat evolved being sufficient to keep the whole boiling for a considerable time.

After heating for about 1½ hours, the product is well cooled and gradually mixed with a further quantity of 23 grams of sodium in 250 grams of absolute alcohol: the same precautions as to temperature being observed as in the first instance. The contents of the flask are again heated in the water-bath, when a further separation of sodium bromide occurs. After boiling for about an hour the alcohol is distilled off, the residue mixed with water, the product extracted twice with a large quantity of ether, and the ethereal solution washed, dried over calcium chloride, and evaporated. The oily product, which should weigh from 155 to 160 grams, is distilled at the ordinary pressure, and the following fractions collected:—

80—200° = about 15 grams.
200—240 = 128—133 grams.
Residue = about 10 grams.

The thermometer rises rapidly to 200°, only small quantities of alcohol, ether, and a little unchanged trimethylene bromide passing over below this temperature, a proof that practically the whole of the ethyl acetoacetate had been converted into ethyl methyldehydrohexonecarboxylate.

The fraction 200—240° is an almost colourless oil, which consists, in spite of the wide range of temperature, of nearly pure ethyl methyldehydrohexonecarboxylate, the yield of which is generally 83 to 86 per cent. of the theoretical, and in some cases, with very careful working, as much as 90 per cent. has been obtained. Its formation by this new method is represented by the equations—

(1.) $CH_3{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_3H_6Br_2 =$
$CH_3{\cdot}CO{\cdot}CH{\cdot}COOC_2H$
$CH_2{\cdot}CH_2{\cdot}CH_2Br.$

(2.) $CH_3{\cdot}C(ONa){:}C{\cdot}COOC_2H_5$
$BrCH_2{\cdot}CH{\cdot}CH_2$
$= CH_3{\cdot}C{=}C{\cdot}COOC_2H_5$
$O<\quad>CH_2 + NaBr.$
$CH_2{-}CH_2$

The high boiling residue left in the retort is probably the product of the action of 2 mols. of ethyl acetoacetate on 1 mol. of trimethylene bromide. It is at present under investigation.

Acetobutyl Bromide, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$.

In preparing acetobutyl bromide, the fractionated ethylic methyldehydrohexonecarboxylate is dissolved in about three times its volume of a saturated solution of hydrogen bromide (sp. gr. about 1·7), and the mixture allowed to stand for 24 hours. The whole is then poured into a large volume of cold water and the precipitated oil separated. The solution still contains a considerable quantity of the bromide, which can be completely extracted with ether if the solution is first neutralised with soda. The separated oil and the ethereal solution are mixed together, washed with dilute sodium carbonate solution, dried over calcium chloride, and the ether distilled off.

The acetobutyl bromide is thus obtained as a brownish oil, the yield of the crude product being about 86 per cent. of the theoretical. The crude bromide is now fractioned under diminished pressure, when the greater portion distils at a constant temperature (under 150 mm. at 155—160°; under 90 mm. at 135—137°), leaving as a residue a dark-brown oil, amounting to about 16 to 20 per cent. of the whole.

Ethyl αω-Diacetylcaproate.

When acetobutyl bromide is warmed with an alcoholic solution of ethyl sodacetoacetate, sodium bromide separates, and ethyl αω-diacetylcaproate is formed, thus:—

$$CH_3\cdot CO\cdot CHNa\cdot COOC_2H_5 + CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br = CH_3\cdot CO\cdot \underset{\displaystyle CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO\cdot CH_3}{\overset{|}{C}}H\cdot COOC_2H_5 + NaBr.$$

In preparing this substance, 80 grams of ethylic acetoacetate were dissolved in a solution of 14 grams of sodium in 150 grams of absolute alcohol, 110 grams of acetobutyl bromide added, and the whole heated on a water-bath in a flask connected with a reflux condenser. As soon as the mixture came to the boiling point, sodium bromide began to separate, and in a very short time the reaction was at an end. The alcohol was distilled off, the residue mixed with water, the product extracted twice with ether, the ethereal solution washed with water, dried over calcium chloride, and the ether evaporated.

The thick, oily residue, which weighed 144 grams, was readily purified by fractionation under reduced pressure.

The pure substance boiling at 238—242° (200 mm. pressure) gave the following result on analysis:—

0·1435 gram substance gave 0·3333 gram CO_2 and 0·1174 gram H_2O.

	Calculated for $C_{12}H_{20}O_4$.	Found.
C	63·16 per cent.	63·34 per cent.
H	8·77 „	9·09 „
O	28·07 „	27·57 „

Ethyl αω-diacetylcaproate is a thick, colourless oil, having a faint odour. It is almost insoluble in water, but readily miscible with ether and alcohol.

Hydrolysis of Ethyl αω-Diacetylcaproate.

The action of caustic potash on ethyl αω-diacetylcaproate may take place in one of the following three ways, according to the conditions of the experiment:—

1st. When the etheral salt is mixed with an excess of a solution of strong potash in methyl alcohol and allowed to stand in the cold, αω-diacetylcaproic acid is formed, thus:—

$$\underset{\displaystyle CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2}{\overset{|}{CH_3\cdot CO\cdot CH}}\cdot COOC_2H_5 + KOH = \underset{\displaystyle CH_2\cdot CO\cdot [CH]_3\cdot CH_2}{\overset{|}{CH_3\cdot CO\cdot CH}}\cdot COOK + C_2H_5\cdot OH.$$

2ndly. When the ethereal salt is hydrolysed by boiling with dilute alcoholic potash, αω-diacetylpentane is formed, thus:—

$$\begin{array}{l} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \end{array} + 2KOH = \begin{array}{l} CH_3\cdot CO\cdot CH_2 \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \\ \alpha\omega\text{-Diacetylpentane.} \end{array} + K_2CO_3 + C_2H_5\cdot OH.$$

3rdly. When the hydrolysis takes place in the presence of a large excess of boiling alcoholic potash, besides αω-diacetylpentane, ω-acetylcaproic acid is formed, thus:—

$$\begin{array}{l} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \end{array} + 2KOH = CH_3\cdot COOK + C_2H_5OH + CH_3\cdot CO\cdot [CH_2]_5\cdot COOK.$$

Potassium ω-acetylcaproate.

αω-Diacetylcaproic Acid, $\begin{array}{l} CH_3\cdot CO\cdot CH\cdot COOH \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \end{array}$.

This acid is prepared by dissolving the crude ethereal salt in an excess of a cold saturated solution of pure potash in methyl alcohol, and allowing the mixture to stand for 24 hours. The resulting slightly brownish solution is placed over sulphuric acid in a vacuum until nearly all the alcohol has evaporated, the residue dissolved in water and repeatedly extracted with ether to remove traces of diacetylpentane which are invariably formed during the reaction. The alkaline solution is carefully acidified with dilute sulphuric acid, the clear liquid extracted several times with pure ether, the ethereal extract dried over calcium chloride and evaporated at a low temperature on a water-bath. The resulting slightly yellowish oil, after the removal of the last traces of ether, consists of nearly pure αω-diacetylcaproic acid, as the following analysis shows:—

0·1769 gram substance gave 0·3886 gram CO_2 and 0·1326 gram H_2O.

	Calculated for $C_{10}H_{16}O_4$.	Found.
C	60·00 per cent.	59·91 per cent.
H	8·00 „	8·33 „
O	32·00 „	31·76 „

Diacetylcaproic acid is miscible with water in all proportions, the solution reacting strongly acid; the addition of a drop of ferric chloride to this solution produces a slight brownish-violet coloration. If a small quantity of the acid is gently heated in a test-tube, car-

bonic anhydride is evolved, and the resulting oil, on distillation, solidifies on the cooler portions of the tube to colourless plates consisting of pure αω-diacetylpentane:—

$$\begin{array}{l} CH_3{\cdot}CO{\cdot}CH{\cdot}COOH \\ CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2 \\ \text{αω-Diacetylcaproic acid.} \end{array} = \begin{array}{l} CH_3{\cdot}CO{\cdot}CH_2 \\ CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2 \\ \text{αω-Diacetylpentane.} \end{array} + CO_2.$$

The salts of diacetylcaproic acid are mostly readily soluble in water and difficult to prepare in a pure condition. The *silver* salt is a colourless, seemingly amorphous compound, readily soluble in cold water. In an aqueous solution of the ammonium salt, ferric chloride produces a light brown precipitate, which is quickly decomposed on heating; lead acetate gives no precipitate in dilute solutions, but copper sulphate produces a light green precipitate readily soluble in warm water. Mercuric nitrate gives a white precipitate which quickly dissolves when the solution is warmed.

αω-Diacetylpentane, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$.

In the first attempts at preparing this diketone, ethyl αω-diacetylcaproate (1 mol.) was mixed in the cold with a dilute solution of potash (2 mols.) in methyl alcohol, and after standing for two days a further quantity of potash (4 mols.) was added, and the mixture boiled for six hours. After distilling off the alcohol, the residue was dissolved in water, the product extracted with ether, the ethereal solution dried over calcium chloride and evaporated. A slightly yellowish oil was obtained containing, besides diacetylpentane, a second substance which is with difficulty separated by fractional distillation. It could be removed, however, by shaking with sodium hydrogen sulphite solution, collecting the solid double compound with diacetylpentane which is formed, washing this with ether, and decomposing with sodium carbonate. In this way a beautiful crystalline substance was obtained which gave the following numbers on analysis:—

0·1528 gram substance gave 0·3890 gram CO_2 and 0·1435 gram H_2O.

	Calculated for $C_9H_{16}O_2$.	Found.
C.....	69·23 per cent.	69·4 per cent.
H.....	10·26 „	10·4 „
O.....	20·51 „	20·2 „

As this process was very inconvenient for the preparation of large quantities of this substance, experiments were made with the object of improving the yield, and as a result the following method was found to give the largest quantity of pure diketone.

Rather more than the calculated quantity of potash required for hydrolysis (2 mols.) is dissolved in a little methyl alcohol, with the addition of a few drops of water; about one third of this solution is mixed with the ethyl diacetylcaproate and the mixture heated to boiling on the water-bath, in a flask connected with a reflux apparatus, for about five minutes, during which operation a quantity of potassic carbonate separates. Another third of the alcoholic potash is now added and the heating continued. In about 10 minutes the remainder of the potash is poured in, the alcohol at once distilled off and the residue mixed with water.

The product is extracted two or three times with ether, the extract dried over calcium chloride, and the ether evaporated. In this way an almost colourless residue is obtained which may readily be purified by fractionation under reduced pressure.

The approximate yield of the crude substance is 50—52 grams from 100 grams ethyl diacetylcaproate. This oil on fractioning behaves somewhat curiously. Thus, under a pressure of 300 mm. the thermometer rises rapidly to 170°, between which temperature and 190° about 5 per cent. distils, as a colourless oil which on cooling shows no signs of solidifying. The distillate between 190° and 219° solidifies entirely, and forms about 90 per cent. of the whole, and on several occasions it was noticed that although the substance gave good numbers on analysis it still possessed no constant boiling point. In order if possible to settle this point, the pure solid substance was refractioned under 240 mm. pressure without, however, any very definite boiling point being noticed. In fractioning large quantities, the nearest approach to a constant boiling point has been 212—215° (300 mm.), and 175—178° (130 mm.).

An analysis of the substance fractioned in this way gave the following numbers:—

0·1725 gram substance gave 0·4367 gram CO_2 and 0·1617 gram H_2O.

	Calculated for $C_9H_{16}O_2$.	Found.
C	69·23 per cent.	69·04 per cent.
H	10·26 „	10·41 „
O	20·51 „	20·55 „

αω-Diacetylpentane, purified by washing with ether on a porous plate, melts at about 48—49°. It is readily soluble in cold ether, alcohol, acetone, chloroform, and warm light petroleum. Small particles thrown on to water move about rapidly with a rotatory motion, and gradually dissolve; but separate again on the addition of potassic carbonate. When shaken for some time with a saturated

solution of hydrogen sodium sulphite, diacetylpentane gradually combines with it to form a solid, semicrystalline substance which was not analysed. This double compound is soluble in cold water, but when heated with water or treated with acids, the diketone separates as an oil which readily solidifies on cooling.

Diacetylpentane dissolves in a concentrated aqueous solution of hydrogen bromide, and on boiling and adding water a heavy oil is precipitated which smells strongly of peppermint; this is at present under investigation. The diketone dissolves very readily and apparently without decomposition in concentrated nitric acid, but on heating nitrous fumes are evolved, and considerable quantities of an acid, apparently oxalic acid, is formed. The solution of diacetylpentane in chloroform absorbs bromine very rapidly, with evolution of streams of hydrogen bromide. After adding the bromine till a permanent coloration was produced, the solution was allowed to evaporate spontaneously; an oily bromide remained which did not solidify even after long standing and was therefore not analysed. $\alpha\omega$-Diacetylpentane dissolves in concentrated sulphuric acid with evolution of heat and formation of a colourless oil which has the composition $C_9H_{14}O$. This substance, which is also formed when the diketone is boiled with alcoholic potash, is of considerable interest, and will be fully described in a subsequent paper. The behaviour of diacetylpentane towards reducing agents is also being carefully investigated, and we hope soon to be able to communicate the results of these investigations to the Society.

$\alpha\omega$-Diacetylpentanedioxime, $CH_3{\cdot}C(NOH){\cdot}[CH_2]_5{\cdot}C(NOH){\cdot}CH_3$.

Before proceeding any further with the investigation of the diacetylpentane it was thought necessary to prove its constitution by the preparation of a dioxime. This substance is readily obtained by treating the diketone in dilute alcoholic solution with a slight excess of hydroxylamine hydrochloride and potassic carbonate. After standing for two days at the ordinary temperature, water was added, the clear solution extracted with ether, the extract washed with water, dried over calcium chloride, and the ether evaporated. The resulting colourless viscid oil was placed over sulphuric acid under diminished pressure, to crystallise. The crystalline cake thus obtained was spread on a porous plate to remove traces of oily mother-liquor, and further purified by recrystallisation from a mixture of benzene and light petroleum.

The analysis gave the following results:—

I. 0·1770 gram substance gave 0·1582 gram H_2O and 0·3764 gram CO_2.

II. 0·1745 gram substance gave 23·3 c.c. N at 16° and 752 mm.

	Calculated for $C_9H_{18}N_2O_2$.	Found. I.	Found. II.
C	58·06 p. c.	57·99	— p. c.
H	9·68 „	9·92	— „
N	15·05 „	—	15·34 „
O	17·21 „	—	—

Diacetylpentanedioxime separates from a mixture of boiling benzene and light petroleum, on cooling, in the form of a crystalline powder. From water, in which it is moderately soluble, it separates in colourless moss-like crystals, melting at 84—85°. It is readily soluble in cold acetone, glacial acetic acid, methyl alcohol, and in warm benzene and ethyl acetate, but only sparingly soluble in boiling and almost insoluble in cold light petroleum. It dissolves freely in cold dilute soda and in concentrated sulphuric acid, forming colourless solutions. When heated in small quantity in a test-tube, it distils with very slight decomposition in the form of a yellowish oil, which quickly solidifies.

ω-Acetylcaproic Acid, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$.

This acid is formed, together with αω-diacetylpentane, when ethyl αω-diacetylcaproate is hydrolysed, as described above, with boiling methyl alcoholic potash, and remains as potassium salt when the diketone is extracted with ether.

To isolate the acid, the alkaline solution is acidified, extracted about 10 times with ether, the ethereal solution dried over calcium chloride, and the ether evaporated. A brown sour-smelling oil is obtained, the quantity of which varies according to the strength of the potash employed. The purification of the crude acid is attended with very considerable loss, as the salts are mostly readily soluble in water, and the acid, when very impure, is almost entirely decomposed when distilled under diminished pressure. Attempts to purify the acid by means of the ethyl salt were also unsuccessful, as when hydrogen chloride is passed into an alcoholic solution of the acid the mixture darkens rapidly, and the product seems to consist of some complicated condensation-compounds containing chlorine.

The acid was obtained in a pure state as follows :—The crude oil is dissolved in excess of boiling baryta, a stream of carbonic anhydride passed through the hot solution, and, after filtering, the solution is acidified and extracted 8 to 10 times with ether. The almost colourless oil which remains, when the ether is distilled, is again dissolved in boiling baryta, and the process repeated. The acid is thus

obtained in the form of a colourless oil, which, however, as was shown by analysis, still contains a large quantity of some compound richer in carbon. It is dissolved in concentrated ammonia, the solution evaporated to dryness at the ordinary temperature, and the residual brownish ammonium salt kept for some time on a porous plate to free it from oily impurities. The colourless salt is dissolved in water, the acidified solution extracted with pure ether, the extract dried over calcium chloride, and evaporated. Acetylcaproic acid remains as a colourless oil, which immediately solidifies to a mass of colourless crystalline plates, melting at 29—30°, and readily soluble in water. This acid has also been obtained by one of us, in conjunction with Dr. Colman, by treating ethyl malonate and sodium ethoxide with acetobutyl bromide, hydrolysing the ethereal salt, and distilling the resulting bibasic acid.

The *silver* salt, $CH_3{\cdot}CO{\cdot}[CH_2]_5{\cdot}COOAg$, prepared by precipitating a neutral aqueous solution of the ammonium salt with silver nitrate, crystallises from boiling water, in which it is very readily soluble, in colourless plates, and, after drying over sulphuric acid, it was analysed with the following results:—

0·2430 gram of the salt gave 0·0985 gram of silver.

	Calculated for $C_8H_{13}O_3Ag$.	Found.
Ag.....	40·68 per cent.	40·53 per cent.

Action of Alcoholic Ammonia on Ethyl αω-Diacetylcaproate.

The first attempts to prepare large quantities of pure diacetylpentane were not attended with much success, and it was thought expedient to try and purify the crude ethyl diacetylcaproate by converting it into a crystalline ammonia compound, analogous to that obtained in the case of ethyl diacetyladipate.

The ethereal salt (42 grams) was therefore dissolved in 8—10 volumes of absolute alcohol, the solution saturated with anhydrous ammonia at the ordinary temperature, and kept for about two days. The solution was again saturated with ammonia, and after keeping for three days the alcohol was evaporated over sulphuric acid. A considerable quantity (6 grams) of a crystalline compound gradually separates from the solution. The crystals were filtered from the mother-liquor, spread on a plate to free them from adherent oil, and then boiled with a mixture of ethyl acetate and methyl alcohol insufficient to dissolve more than about half the whole. The residue was completely dissolved in a mixture of ethyl acetate and methyl alcohol, and the crystalline compound which separated on cooling, recrystallised from methyl alcohol. A compound, $C_{10}H_{15}O_2N$, is thus

obtained in compact colourless crystals, which, after drying over sulphuric acid, gave the following results on analysis:—

I. 0·1648 gram of substance gave 0·3994 gram CO_2 and 0·1280 gram H_2O.

II. 0·0917 gram substance gave 5·95 c.c. N at 12° and 750 mm.

	Calculated for $C_{10}H_{15}O_2N$.	Found. I.	Found. II.
C	66·3 p. c.	66·1	— p. c.
H	8·3 „	8·6	— „
N	7·7 „	—	7·6 „
O	17·7 „	—	—

This substance, as will be shown hereafter, is most probably dehydrodiacetylcapronamide, and has the constitution—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}C\begin{matrix}CMe\\CO-\end{matrix}>NH.$$

It separates from cold methyl alcohol in large compact crystals, which have been very kindly measured by Professor Haushofer, who gives the following account of his observations:—

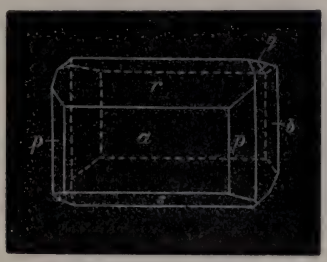
" Crystalline form *monoclinic*.

$$a : b : c = 0{\cdot}7487 : 1 : 0{\cdot}3997.$$

$$\beta = 79° 11'.$$

Plates or small prisms of the combination $\infty\breve{P}\infty(100) = a$, $\infty\breve{P}\infty(010) = b$, $-\breve{P}\infty(101) = r$, $\breve{P}\infty(10\bar{1}) = s$, $\infty P(110) = p$, very small, occurring seldom and difficult to measure; $2\breve{P}\infty(021) = q$.

	Observed.	Calculated.
$a : r = (100)(101) =$	126° 18′	—
$a : s = (100)(10\bar{1}) =$	109 26	—
$a : p = (100)(110) =$	126 20	—
$r : s' = (101)(\bar{1}01) =$	124 19	124° 16′
$r : s = (101)(10\bar{1}) =$	55 49	55 44
$q : s' = (021)(\bar{1}01) =$	approx. 133	132 48
$q : r = (021)(101) =$	„ 136	135 14 "



The plane of the optical axes is the plane of symmetry; one axis meets the surface *a*, the other surface *s*, both apparently near the edge *a*/*s*.

Dehydrodiacetylcapronamide melts at 233—235° with previous softening and slight decomposition, and when heated in small quantities at a higher temperature, it is decomposed with evolution of ammonia, or some volatile base. It is readily soluble in cold glacial acetic acid and in mineral acids, and moderately soluble in hot methyl alcohol and ethyl acetate, but only sparingly in cold benzene, and almost insoluble in boiling acetone. When boiled with water it gradually dissolves, and is partially converted into diacetylcapronamide, which is much more readily soluble; on cooling, a considerable quantity of the dehydro-compound separates immediately in beautiful, short, thick, transparent plates, and the filtrate contains the amide, which separates slowly in flat, transparent, efflorescent plates, when the solution is allowed to evaporate at the ordinary temperature. It is slowly decomposed when boiled with soda, considerable quantities of ammonia being evolved, and the characteristic peppermint smell of the compound $C_9H_{14}O$ being distinctly perceptible.

The constitution of this compound seems to be proved by the following experiments:—

(1.) It yields an acetyl-derivative and a nitroso-compound.

(2.) It is readily hydrolysed by cold alcoholic potash, being converted into $\alpha\omega$-diacetylcaproic acid.

(3.) When boiled with water, it takes up 1 mol. H_2O, yielding diacetylcapronamide.

Acetyldehydrodiacetylcapronamide, $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}C{\lessgtr}^{CMe}_{CO-}{>}NAc$.

When dehydrodiacetylcapronamide is boiled with excess of acetic anhydride for about four hours, it is converted into an acetyl-derivative. To isolate the product, the acetic anhydride is partially removed by distillation, the residue mixed with water, and after keeping for some time the whole extracted two or three times with ether. The ethereal solution is washed with water and sodium carbonate solution until free from acetic acid, dried over calcium chloride, and the ether evaporated.

Acetyldehydrodiacetylcapronamide remains as an almost colourless oil, and as it could not be obtained in a crystalline condition, the crude product was kept over sulphuric acid for about two days and then analysed, with the following results:—

0·1535 gram of substance gave 0·3585 gram CO_2 and 0·1070 gram H_2O.

	Calculated for $C_{12}H_{17}O_3N$.	Found.
C	64·57 per cent.	63·70 per cent.
H	7·62 „	7·74 „
N.....	6·28 „	—
O	21·53 „	—

A nitroso-compound was prepared, in small quantity, by treating a cold dilute hydrochloric acid solution of dehydrodiacetylcapronamide with the calculated quantity of sodium nitrite, and extracting the product with ether. A colourless oil was obtained; it dissolved in soda with a transient yellow coloration, but owing to the small quantity at our disposal it was not analysed.

Dehydrodiacetylcapronamide is decomposed by a cold concentrated solution of alcoholic potash, yielding ammonia and $\alpha\omega$-diacetylcaproic acid. A small quantity of the dehydro-compound was dissolved in cold methyl alcoholic potash, the solution kept for two days, and the alcohol evaporated at the ordinary temperature. The residue was dissolved in water, the solution extracted with ether to remove any diacetylpentane which might have been formed, then acidified with dilute sulphuric acid, and the acid extracted with pure ether. A colourless oil remained when the dried ethereal solution was evaporated, and the crude product, after keeping for 24 hours over sulphuric acid, was analysed with the following results:—

0·1703 gram of substance gave 0·3748 gram CO_2 and 0·1288 gram H_2O.

	Calculated for $C_{10}H_{16}O_4$.	Found.
C.....	60·0 per cent.	60·0 per cent.
H	8·0 „	8·4 „
O.....	32·0 „	31·6 „

That this acid is in reality diacetylcaproic acid is further proved by the following experiments:—When heated at about 100°, rapid evolution of carbonic anhydride occurs, and on heating more strongly the whole distils in the form of a colourless oil, and quickly solidifies. The solid distillate was found to be identical with diacetylpentane, and, like the last-named compound, on boiling with potash it gives out a strong smell of peppermint, due to the formation of the compound $C_9H_{14}O$. When the dehydro-compound is boiled with water, it is converted into diacetylcapronamide.

$\alpha\omega$-Diacetylcapronamide, $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}CH(COMe){\cdot}CONH_2$.

This amide is most probably formed, together with its dehydro-derivative, when ethyl diacetylcaproate is treated with alcoholic ammonia as described above; but as the two compounds show great

similarity in their behaviour towards most solvents, they cannot easily be separated by fractional crystallisation. The amide is best prepared in a pure state by boiling the dehydro-compound for some time with water, separating the unchanged dehydrodiacetylcapronamide which crystallises from the solution on cooling, and allowing the solution to evaporate at the ordinary temperature. Diacetylcapronamide separates slowly in long, thick, transparent needles, or in flat, transparent, oblong plates containing 2 mols. of water of crystallisation. It loses its water when kept over sulphuric acid, and two determinations, made with different samples, gave the following results:—

I. 0·6219 gram of substance, dried between blotting-paper, lost 0·0944 gram over sulphuric acid.

II. 0·6195 gram substance, dried for a short time on a porous plate, lost 0·0995 gram over sulphuric acid.

	Calculated for $C_{10}H_{17}O_3N + 2H_2O$.	Found. I.	Found. II.
H_2O	15·3 p. c.	15·18	16·04 p. c.

The anhydrous substance was analysed and gave the following results:—

0·1744 gram substance gave 0·3871 gram CO_2 and 0·1414 gram H_2O.

	Calculated for $C_{10}H_{17}O_3N$.	Found.
C	60·30 per cent.	60·53 per cent.
H	8·54 „	9·0 „
N	7·03 „	—

Diacetylcapronamide crystallises from dilute methyl alcohol in flat, transparent plates which effloresce, becoming opaque and very brittle

on exposure to the air. Some of these crystals were measured with a microscope provided with a graduated circle, and the observations made with one very well-defined crystal are given below.

Diacetylcapronamide has no well-defined melting point, as when heated to about 200° it begins to soften, and does not melt completely until 228°. It is readily soluble in cold methyl alcohol and in glacial acetic acid, but only moderately so in cold ethyl alcohol or water, and very sparingly in benzene, chloroform, ether, and acetone. It dissolves freely in warm, concentrated sulphuric acid, and is not precipitated when the solution is diluted; when boiled with soda, ammonia is evolved, and the characteristic smell of the compound $C_9H_{14}O$ is perceptible.

In studying the formation of dehydrodiacetylcapronamide from diacetylcapronamide, it is evident that the former substance may have either of the following formulæ:—

I. II.

$$CH_3\cdot CO\cdot[CH_2]_4\cdot CH<\begin{matrix}CMe\\CO-\end{matrix}>N \qquad CH_3\cdot CO\cdot[CH_2]_4\cdot C<\begin{matrix}CMe\\CO-\end{matrix}>NH.$$

The formation of a substance represented by Formula I is easily understood from the following equation:—

$$CH_3\cdot CO\cdot[CH_2]_4\cdot\overset{\overset{CO\cdot Me}{|}}{C}H\cdot CO\cdot NH_2 - H_2O = CH_3\cdot CO\cdot[CH_2]_4\cdot CH<\begin{matrix}CMe\\CO-\end{matrix}>N.$$

Diacetylcapronamide.

In the case of Formula II it is necessary to suppose that diacetylcapronamide is first converted into its labile modification. The subsequent elimination of water taking place thus:—

$$CH_3\cdot CO\cdot[CH_2]_4\cdot\overset{\overset{C(OH)Me}{||}}{C}\cdot CO\cdot NH_2 - H_2O = CH_3\cdot CO\cdot[CH_2]_4\cdot C<\begin{matrix}CMe\\CO-\end{matrix}>NH.$$

Diacetylcapronamide (labile form).

That Formula II represents the constitution of dehydrodiacetylcapronamide is proved by the fact that this substance yields an acetyl- and a nitroso-compound, and that on hydrolysis it is converted into diacetylcaproic acid.

The oily mother-liquors from which dehydrodiacetylcapronamide crystallises, were kept for a long time over sulphuric acid, but no further separation of crystals took place. The oil was therefore distilled under diminished pressure; considerable decomposition occurred, large quantities of ammonia and other gases being evolved, and a yellow oil collected in the receiver. The distillate was then

submitted to fractional distillation, but again considerable decomposition took place, and the resulting oily product seemed to consist of a mixture of several compounds, the separation of which has not yet been attempted.

In the course of our experiments on the behaviour of diacetylpentane towards dehydrating agents, a compound was obtained, the formation of which from the diketone might possibly be due to internal change in one of the $-CH_2\cdot CO-$ groups. At an early stage of this investigation it was deemed important to prepare a diketone analogous to diacetylpentane in which methyl was substituted for one of the hydrogen atoms in one of the $-CH_2\cdot CO-$ groups. Such a diketone should be obtained by treating the sodium compound of ethyl methylacetoacetate with acetobutyl bromide and hydrolysing the resulting ethyl α-methyl-$\alpha\omega$-diacetylcaproate; thus:

(1) $CH_3\cdot CO\cdot CNa(CH_3)\cdot COOC_2H_5 + CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br$

$= \begin{matrix} CH_3\cdot CO\cdot C(CH_3)\cdot COOC_2H_5 \\ | \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \end{matrix} + NaBr.$

(2) $\begin{matrix} CH_3\cdot CO\cdot C(CH_3)\cdot COOC_2H_5 \\ | \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2 \end{matrix} + 2KOH$

$= CH_3\cdot CO\cdot [CH_2]_4\cdot CH(CH_3)\cdot CO\cdot CH_3 + K_2CO_3 + C_2H_5\cdot OH.$

We append a brief account of the experiments which were carried out with this object.

Ethyl α-Methyl-$\alpha\omega$-Diacetylcaproate,

$$\begin{matrix} CH_3\cdot CO\cdot C(CH_3)\cdot COOC_2H_5 \\ | \\ CH_3\cdot CO\cdot [CH_2]_3\cdot CH_2. \end{matrix}$$

In preparing this substance, ethyl methylacetoacetate (32 grams) was gradually added to a cold solution of sodium (5·1 grams) in absolute alcohol (60 grams), acetobutyl bromide (40 grams) poured in, and the whole heated to boiling for about three hours. The alcohol was then distilled off, the residue mixed with water, and extracted several times with ether, the extract dried over calcium chloride, and the ether distilled off. The residual oil (57 grams) on fractioning under reduced pressure (220 mm.) separated into two portions boiling at 109—205° and 205—270° respectively. The higher boiling fraction was again distilled, and the portion boiling at 255—260° analysed with the following results:—

	Calculated for $C_{13}H_{22}O_4$.	Found.
C.....	64·46 per cent.	64·94 per cent.
H.....	9·09 „	9·41 „
O.....	26·45 „	25·65 „

Ethyl α-methyl-$\alpha\omega$-diacetylcaproate is a colourless oil possessing a faint odour. It is insoluble or nearly insoluble in water, but mixes with alcohol and ether in all proportions.

α-Methyl-$\alpha\omega$-Diacetylpentane, $CH_3{\cdot}CO{\cdot}[CH_2]_4{\cdot}CHMe{\cdot}CO{\cdot}CH_3$.

In preparing this substance, 18 grams of the ethereal salt were mixed with a solution of 10 grams of pure potash in alcohol and heated for a short time on a water-bath. The decomposition set in almost immediately—much potassic carbonate separating out. After boiling for about an hour, the alcohol was distilled off, the residue mixed with water, and the alkaline product extracted two or three times with ether. The ethereal solution after drying over calcium chloride and evaporating, deposited a quantity of an almost colourless oil which on repeated distillation under diminished pressure (350 mm.), boiled fairly constantly at 232—235°. This fraction was analysed with the following results :—

0·1705 gram substance gave 0·4400 gram CO_2 and 0·1632 gram H_2O.

	Calculated for $C_{10}H_{18}O_2$.	Found.
C.....	70·59 per cent.	70·38 per cent.
H.....	10·59 „	10·64 „
O.....	18·82 „	18·98 „

α-Methyl-$\alpha\omega$-diacetylpentane is a colourless, mobile oil, which even after long standing shows no signs of crystallisation; as it has frequently been noticed that methyl-derivatives of substances containing normal chains melt at a lower temperature than the substances themselves, methyldiacetylpentane might be expected to be an oil at the ordinary temperature. The diketone dissolves in a saturated solution of sodium hydrogen sulphite, and is reprecipitated on adding potassic carbonate, but no crystalline double compound was formed, as in the case of diacetylpentane.

The alkaline solution, from which the diketone was separated by extraction with ether, contains considerable quantities of an oily acid, probably α-methyl-ω-acetylcaproic acid.

Dibenzoylpentane.

The results of experiments on the behaviour of diacetylpentane towards dehydrating agents made it necessary to determine whether either of the methyl-groups in this substance took part in the formation of the compound $C_9H_{14}O$, which has been referred to above. If a diketone analogous to diacetylpentane, but containing two phenyl-groups in place of the methyl radicles, was treated with dehydrating agents under the same conditions as those employed in the case of diacetylpentane, the results might be of considerable value in ascertaining the constitution of the compound $C_9H_{14}O$.

With this view we treated benzoylbutyl bromide with ethyl sodobenzoylacetate in alcoholic solution, and obtained ethyl $\alpha\omega$-dibenzoylcaproate, the reaction taking place in accordance with the equation—

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br + C_6H_5\cdot CO\cdot CHNa\cdot COOEt = C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(COPh)\cdot COOEt + NaBr.$$

When this ethereal salt is hydrolysed with alcoholic potash, it yields $\alpha\omega$-dibenzoylpentane, potassium ω-benzoylcaproate, potassium benzoate, and potassium carbonate—

$$C_6H_5\cdot CO\cdot[CH_2]_4\cdot CH(COPh)\cdot COOEt + 2KOH = C_6H_5\cdot CO\cdot[CH_2]_5\cdot CO\cdot C_6H_5 + K_2CO_3 + C_2H_5\cdot OH \text{ and}$$

$$C_6H_5\cdot CO\cdot[CH_2]_4\cdot CH(COPh)\cdot COOEt + 2KOH = C_6H_5\cdot CO\cdot[CH_2]_5\cdot COOK + C_6H_5\cdot COOK + C_2H_5\cdot OH.$$

The benzoylbutyl bromide employed in these experiments was prepared by treating phenyldehydrohexone with concentrated hydrobromic acid, as has been previously described by one of us (Trans., 1887, 732). The crystalline product is dissolved in ether, the solution washed with dilute sodium carbonate solution until free from hydrobromic acid, dried over calcium chloride, and the ether evaporated. The benzoylbutyl bromide is thus obtained almost perfectly pure and quite colourless, and can be directly employed for the preparation of ethyl dibenzoylcaproate.

Ethyl $\alpha\omega$-Dibenzoylcaproate, $C_6H_5\cdot CO\cdot[CH_2]_4\cdot CH(COPh)\cdot COOEt$.

To a solution of 2·8 grams of sodium in absolute alcohol 24 grams of ethyl benzoylacetate are gradually added, care being taken to keep the temperature below 40°; a slightly warm alcoholic solution of 28·8 grams of benzoylbutyl bromide is then poured in, and the

mixture heated on the water-bath with reflux condenser. Just as the alcohol begins to boil, the separation of sodium bromide commences, and after heating for about two hours the reaction is at an end. The alcohol is removed by distillation, the residue mixed with water, the product extracted with ether, and the ethereal solution dried and evaporated. Ethyl dibenzoylcaproate (about 42 grams) remains as a yellowish oil, and if the substances employed in the reaction are carefully weighed, the product is almost perfectly pure, as is shown by the following analysis, made with a sample which had been kept for a few days over sulphuric acid :—

0·1738 gram substance gave 0·4762 gram CO_2 and 0·1112 gram H_2O.

	Calculated for $C_{22}H_{24}O_4$.	Found.
C	75·0 per cent.	74·7 per cent.
H	6·8 „	7·1 „
O	18·2 „	18·2 „

It is a thick, yellowish oil, with an aromatic odour, and insoluble in water; even when kept for some weeks, it showed no signs of solidifying. When boiled with alcoholic potash, it is quickly hydrolysed and decomposed in accordance with the above equations.

$\alpha\omega$-Dibenzoylpentane, $C_6H_5{\cdot}CO{\cdot}[CH_2]_5{\cdot}CO{\cdot}C_6H_5$.

This diketone is best prepared from the ethereal salt by a method similar to that employed in the preparation of diacetylpentane. The crude ethyl dibenzoylcaproate (20 grams) is boiled for a short time with a solution of potash in methyl alcohol (= 10 grams KOH), this being added in small portions at a time as already described. The alcohol is distilled off, the residue treated with water to dissolve the sodium bromide, the oil extracted with ether, and the ethereal solution dried and evaporated. The diketone (14 grams) remains in the form of a thick, yellow oil, which quickly solidifies on cooling; after spreading on a porous plate to remove impurities, it was recrystallised from hot, dilute methyl alcohol, dried over sulphuric acid, and analysed.

0·1796 gram of substance gave 0·5347 gram CO_2 and 0·1150 gram H_2O.

	Calculated for $C_{19}H_{20}O_2$.	Found.
C	81·43 per cent.	81·20 per cent.
H	7·14 „	7·11 „
O	11·43 „	11·69 „

$\alpha\omega$-Dibenzoylpentane crystallises from dilute methyl alcohol in long, colourless needles, melts at 67—68°, and when heated in small quantities under the ordinary pressure it distils at a temperature above 300° with only very slight decomposition. It is very readily soluble in cold acetone, but is precipitated in microscopic needles on adding water; it dissolves freely in cold benzene and ether, but is only moderately soluble in cold alcohol and seemingly insoluble in hot or cold water. It is readily soluble in warm, light petroleum (70—90°), and on cooling it separates from the solution almost completely in very slender needles.

Experiments on the behaviour of this diketone towards reducing and dehydrating agents are in progress.

Dibenzoylpentanedioxime, $C_6H_5{\cdot}C(NOH){\cdot}[CH_2]_5{\cdot}C(NOH){\cdot}C_6H_5$.

The dioxime was prepared by treating the diketone in alcoholic solution with hydroxylamine hydrochloride and a large excess of potash as recommended by Auwers (*Ber.*, **22**, 604). After keeping for two days the alcohol was distilled off, the residue mixed with water, and the solid substance which was precipitated separated by filtration and dried on a porous plate. It was then boiled with a small quantity of benzene to remove any unchanged diketone, the residue recrystallised from methyl alcohol, and dried at 100°. A nitrogen determination was made with the following result:—

0·1701 gram substance gave 13·4 c.c. of nitrogen measured at 15° and 736 mm.

	Calculated for $C_{19}H_{22}O_2N_2$.	Found.
N	9·03 per cent.	9·23 per cent.

It crystallises from boiling methyl alcohol in small, glistening needles, melts at 175—176°, and is readily soluble in hot acetone and glacial acetic acid, but only very sparingly in boiling benzene, from which it separates in the form of a crystalline powder. It is very sparingly soluble in potash, but dissolves moderately easily in concentrated hydrochloric acid, yielding a colourless solution from which it is precipitated on adding water.

The alkaline filtrate from the dioxime, on acidifying with dilute sulphuric acid, gave a small quantity of a colourless substance which, after recrystallising from methyl alcohol, melted at 168—169° with previous softening, and consisted probably of slightly impure dioxime.

ω-Benzoylcaproic Acid, $C_6H_5 \cdot CO \cdot [CH_2]_5 \cdot COOH$.

The alkaline solutions from which αω-dibenzoylpentane had been extracted as described above contain potassium ω-benzoylcaproate and potassium benzoate. The free acids are precipitated on adding dilute sulphuric acid as an oil, which soon solidifies and can be separated by filtration. The quantity of the crude product obtained depends on the concentration of the alcoholic potash employed. In one experiment 20 grams of the ethereal salt was hydrolysed with an alcoholic solution of 10 grams of potash, and the crude acid mixture weighed 2 grams; in another experiment 40 grams of ethyl dibenzoylcaproate were treated with 40 grams of potash in methyl alcoholic solution and 12 grams of crude acids were obtained.

In order to remove the benzoic acid, the mixture (7 grams) is heated on a watch-glass at 100° until the weight becomes constant, which is the case after about 10 hours, and the residue (4·5 grams) recrystallised twice from light petroleum. The pure compound melted at 81—82°, and gave the following results on analysis:—

0·1449 gram substance gave 0·3773 gram CO_2 and 0·0986 gram H_2O.

	Calculated for $C_{13}H_{16}O_3$.	Found.
C	70·90 per cent.	71·01 per cent.
H	7·27 „	7·56 „
O	21·83 „	21·43 „

ω-Benzoylcaproic acid crystallises from boiling light petroleum in long, glistening, transparent, plates and from boiling water, in which it is only sparingly soluble, in slender, microscopic needles. It is very readily soluble in cold methyl alcohol, ethyl alcohol, ethyl acetate, and benzene, but only moderately soluble in boiling light petroleum, and almost insoluble in the cold.

The *silver* salt was prepared by precipitating a neutral, aqueous solution of the ammonium salt with silver nitrate, washing the precipitate with cold water, and drying over sulphuric acid. Analysis:—

0·3604 gram of the salt gave 0·1186 gram of silver.

	Calculated for $C_{13}H_{15}O_3Ag$.	Found.
Ag	32·97 per cent.	32·91 per cent.

It is a colourless, seemingly amorphous compound, very sparingly soluble in boiling water, which does not darken on exposure to light; when heated, it turns a beautiful peacock-green.

The *cadmium* salt, prepared by treating an aqueous solution of the ammonium salt with cadmium chloride, separates from hot water in colourless microscopic needles. Mercuric nitrate produces in aqueous solutions of the ammonium salt a colourless, flocculent precipitate which is soluble in boiling water. Lead acetate gives a white, amorphous precipitate, copper sulphate a bluish-green precipitate, and ferric chloride a flesh-coloured precipitate. The barium salt and the calcium salt are granular, crystalline compounds readily soluble in hot water.

Oxime of ω-Benzoylcaproic Acid, $C_6H_5{\cdot}C(NOH){\cdot}[CH_2]_5{\cdot}COOH$.

ω-Benzoylcaproic acid, dissolved in alcohol, was treated with hydroxylamine hydrochloride and a large excess of potash, and the solution kept for two days at the ordinary temperature. The alcohol was then partially distilled, the residue mixed with water, acidified with dilute hydrochloric acid, and the precipitated oil extracted with ether; the ethereal solution was washed once or twice with dilute hydrochloric acid, and then with water, dried, and the ether evaporated. The oxime remained as a yellowish oil, which, when kept over sulphuric acid under diminished pressure, gradually solidified. It was spread on a porous plate, washed with a little light petroleum, dissolved in cold benzene, and precipitated from the solution with light petroleum.

The oxime of benzoylcaproic acid is thus obtained in colourless, microscopic needles melting at about 75°. A nitrogen determination gave the following results:—

0·1996 gram substance gave 10·25 c.c. N at 14° and 740 mm.

	Calculated for $C_{13}H_{17}O_3N$.	Found.
N	5·96 per cent.	5·88 per cent.

It is very readily soluble in ether and cold benzene, but only sparingly in hot water, and almost insoluble in cold light petroleum. It dissolves freely in caustic alkalis and in concentrated hydrochloric acid, but it is partially reprecipitated when the acid solution is diluted.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, February*, 1890. Vol. LVII.]

$\alpha\omega$-DIACETYL-$\alpha\omega$-DIETHYLPENTANE.

By F. Stanley Kipping, Ph.D., DSc., and W. H. Perkin, jun., Ph.D.

In the preceding paper we have described the preparation of a compound of the composition $C_9H_{14}O$, and have given an account of various experiments, from the results of which it seems to be proved that this substance is methyltetrahydrobenzene methyl ketone,

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot CO\cdot CH_3.$$

In order to distinguish between several of the theoretically possible formulæ for this compound (compare p. 14), it became necessary to prepare a diketone of the formula $R\cdot CO\cdot CHR\cdot[CH_2]_3\cdot CHR\cdot CO\cdot R$, and to study its behaviour under the same conditions as those employed in the preparation of the compound $C_9H_{14}O$ from $\alpha\omega$-diacetylpentane, $COMe\cdot[CH_2]_5\cdot COMe$.

A short account of these experiments will, we hope, not be without some interest.

When ethyl ethylacetoacetate (2 mols.) is treated with sodium ethoxide (2 mols.) and trimethylene bromide (1 mol.) in alcoholic solution, a moderately energetic reaction occurs on warming gently, and, after proceeding in the usual manner, a yellow oil is obtained.

The crude product, which consists of several compounds, contains about 40—45 per cent. of ethyl $\alpha\omega$-diacetyl-$\alpha\omega$-diethylpimelate, $COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt$, produced by the combination of 1 mol. of trimethylene bromide with 2 mols. of ethyl sodioethylacetoacetate in accordance with the equation—

$$2CH_3\cdot CO\cdot CNaEt\cdot COOEt + C_3H_6Br_2 = COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt + 2NaBr.$$

This ethereal salt is readily hydrolysed when boiled with alcoholic potash, the principal products being $\alpha\omega$-diacetyl-$\alpha\omega$-diethylpentane and ω-acetyl-$\alpha\omega$-diethylcaproic acid. The equations representing the decomposition are as follows :—

$$COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt + 4KOH = COMe\cdot CHEt\cdot[CH_2]_3\cdot CHEt\cdot COMe + 2K_2CO_3 + 2C_2H_5\cdot OH,$$

and

$$COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt + 4KOH = COMe\cdot CHEt\cdot[CH_2]_3\cdot CHEt\cdot COOK + 2C_2H_5\cdot OH + K_2CO_3 + CH_3\cdot COOK.$$

It seems probable that, in addition to the two compounds referred to above, small quantities of αω-diethylpimelic acid are also produced by the following reaction:—

$$COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt + 4KOH = COOK\cdot CHEt\cdot[CH_2]_3\cdot CHEt\cdot COOK + 2C_2H_5\cdot OH + 2CH_3\cdot COOK.$$

Action of Trimethylene Bromide on Ethyl Sodioethylacetoacetate.

Formation of Ethyl αω-Diacetyl-αω-diethylpimelate, $COOEt\cdot CEt(COMe)\cdot[CH_2]_3\cdot CEt(COMe)\cdot COOEt$.

Ethyl diacetyldiethylpimelate is obtained, together with considerable quantities of compounds of lower boiling point, when ethyl sodioethylacetoacetate is treated with an alcoholic solution of trimethylene bromide.

Ethyl ethylacetoacetate (2 mols.) is added, in small quantities at a time, to a solution of sodium (1 mol.) in about 12 times its weight of alcohol, the temperature being kept below 25—30° by cooling under the tap from time to time; after adding the trimethylene bromide (1 mol.), the mixture is heated on the water-bath in a flask provided with a reflux condenser. As soon as the temperature rises to about 70—80°, an energetic reaction commences, sodium bromide separates from the solution, and the heat developed is sufficient to keep the alcohol in ebullition for several minutes. After heating for 2—3 hours to complete the reaction, the alcohol is evaporated, the residue mixed with water, and the precipitated oil extracted with ether. When the ethereal extract is evaporated, there remains a yellow oil, the quantity of which is about equal to that of the ethyl ethylacetoacetate employed.

The crude product is distilled with steam as quickly as possible, the distillation being continued as long as oily drops collect in the receiver. In this way the ethyl diacetyldiethylpimelate, which forms from 40 to 45 per cent. of the whole, is separated from the more volatile compounds. The dark yellow oil which remains in the flask is extracted with ether, the ethereal solution dried over calcium chloride and evaporated. That this process of separation is very efficient is shown by the following analysis, which was made with a portion of the residual oil after it had been kept over sulphuric acid under reduced pressure for about 24 hours.

0·1474 gram of substance gave 0·3430 gram of CO_2 and 0·1220 gram of H_2O.

	Calculated for $C_{19}H_{32}O_6$.	Found.
C	64·05 per cent.	63·46 per cent.
H	8·99 „	9·22 „
O	26·96 „	27·32 „

When the crude ethyl diacetyldiethylpimelate is distilled under reduced pressure (45—50 mm.), the thermometer rises rapidly to about 205°, then a little more slowly to 235°; almost the whole distils between 235° and 255°, a small quantity only passing over between 255° and 280°. The oil boiling at 235—255° was fractionated again under the same pressure, and the portion boiling constantly at 249—252° collected separately.

This fraction quickly solidifies to a mass of colourless crystals, and after having been spread on a porous plate to free it from traces of oily impurities, it melted at 42—43° with previous softening.

The analyses of the crystalline compound purified in this way gave the following results:—

I. 0·2109 gram of substance gave 0·4937 gram of CO_2 and 0·1689 gram of H_2O.

II. 0·2500 gram of substance gave 0·5840 gram of CO_2 and 0·2016 gram of H_2O.

	Calculated for $C_{19}H_{32}O_6$.	Found. I.	Found. II.
C	64·05 per cent.	63·80	63·71 per cent.
H	8·99 „	8·90	8·96 „
O	26·96 „	27·30	27·33 „

Ethyl diacetyldiethylpimelate separates from ether and alcohol in long. very slender needles melting at 44—45° with slight previous softening; it is very readily soluble both in ether and in alcohol, so that it cannot well be purified by crystallisation from these solvents. On adding water to a cold alcoholic solution, the ethereal salt is precipitated in an oily condition, but it almost immediately solidifies to a mass of ill-defined crystals. It is very readily soluble in benzene, light petroleum, xylene, chloroform, and most ordinary solvents, but it seems to be quite insoluble in cold water. Ferric chloride produces no coloration in alcoholic solutions. It is readily hydrolysed by warm alcoholic potash, the principal product being acetyldiethylcaproic acid. When treated with concentrated alcoholic potash in the cold, it is slowly decomposed; the solution contains small quantities of diacetyldiethylpentane, and the potassium salt of a thick, colourless acid, probably diacetyldiethylpimelic acid, which is mixed with some other acid richer in carbon.

Bye-products obtained in the preparation of Ethyl Diacetyldiethylpimelate.

The crude product of the action of trimethylene bromide on ethyl sodioethylacetoacetate contains, as has been stated above, a considerable proportion (55—60 per cent.) of an oil which can be separated from the ethyl diacetyldiethylpimelate by distilling with steam; when the distillate is extracted with ether, and the extract dried over calcium chloride and evaporated, a yellowish, mobile oil with a pleasant ethereal odour is obtained. This oil is probably a mixture of unchanged ethyl ethylacetoacetate and ethyl ethylallylacetoacetate; the last-named compound would probably be produced by the interaction of the trimethylene bromide and ethyl sodioethylacetoacetate according to the equations—

$$CH_3{\cdot}CO{\cdot}CEtNa{\cdot}COOEt + C_3H_6Br_2 = CH_3{\cdot}CO{\cdot}CEt{\cdot}(COOEt){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br \text{ and}$$

$$CH_3{\cdot}CO{\cdot}CEt(COOEt){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br + CH_3{\cdot}CO{\cdot}CEtNa{\cdot}COOEt = CH_3{\cdot}CO{\cdot}CEt(COOEt){\cdot}CH_2{\cdot}CH{:}CH_2 + CH_3{\cdot}CO{\cdot}CHEt{\cdot}COOEt + NaBr.$$

It was repeatedly submitted to fractional distillation under the ordinary pressure in order to try and isolate the ethyl ethylallylacetoacetate, but the attempt was unsuccessful. Various fractions were analysed, but in all cases the results agreed with those required by a mixture of ethyl ethylacetoacetate and ethyl ethylallylacetoacetate, the analyses giving from 64·4 to 65·3 per cent. of carbon and about 9·1 per cent. of hydrogen instead of 66·7 per cent. of carbon and 9·0 per cent. of hydrogen as required by ethyl ethylallylacetoacetate.

αω-Diacetyl-αω-diethylpentane, $CH_3{\cdot}CO{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}CO{\cdot}CH_3$

Diacetyldiethylpentane is best prepared by treating ethyl diacetyldiethylpimelate with alcoholic potash as described in the preparation of diacetylpentane.

The ethereal salt is dissolved in a small quantity of alcohol, and the solution heated to boiling in a flask provided with a reflux condenser; about one-third of a hot, moderately concentrated, alcoholic solution of potash (4 mols.) is then added, and the mixture is boiled again. As soon as no further separation of potassium carbonate occurs, another third of the potash solution is poured in and the mixture is heated again for about 10 minutes; the remainder of the alcoholic potash is then added and the alcohol is immediately evaporated. The alkaline residue is mixed with water, the precipitated diketone

extracted with ether, the ethereal solution dried over potassium carbonate and evaporated. The yellowish-brown, mobile oil which is thus obtained consists of impure diacetyldiethylpentane; the quantity of the crude product is only 11—12 grams from 50 grams of the ethereal salt, the small yield being due to the formation of large quantities of acid decomposition-products.

As the crude diketone showed no signs of crystallisation even when cooled below 0°, it was submitted to fractional distillation under a pressure of 110 mm. The thermometer rose rapidly to about 160°, and about 10 per cent. of the whole distilled below 206°; the thermometer then remained very constant at 207—208°, about 50 per cent. passing over between 200° and 210°, and the remainder at a slightly higher temperature.

The fraction 200—210° was distilled again under the same pressure and the portion boiling at 207—208° collected separately. This liquid on analysis gave the following results:—

0·1690 gram of substance gave 0·4533 gram of CO_2 and 0·1751 gram of H_2O.

	Calculated for $C_{13}H_{24}O_2$.	Found.
C	73·59 per cent.	73·10 per cent.
H	11·32 „	11·32 „
O	15·09 „	15·58 „

Diacetyldiethylpentane is a colourless, moderately mobile oil with a slight, rather pleasant, aromatic odour similar to that of diacetylpentane. It boils at 207—208° (110 mm.), and shows no signs of crystallising. It is insoluble or only very sparingly soluble in water, but miscible with alcohol, ether, and other ordinary solvents in all proportions. It does not combine with sodium hydrogen sulphite even when left for a long time in contact with a concentrated aqueous solution of the salt. It dissolves in cold concentrated sulphuric acid with a yellowish-brown coloration, but it undergoes no change even after two days' time, as is proved by the experiments described below.

$\alpha\omega$-Diacetyl-$\alpha\omega$-diethylpentanedioxime,
$NOH{:}CMe{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}CMe{:}NOH$.

Diacetyldiethylpentane combines readily with hydroxylamine in alkaline solution, yielding the dioxime.

The diketone (about 1 gram) is dissolved in alcohol, treated with an alcoholic solution of hydroxylamine hydrochloride (1·5 gram) and potash (5 grams), and the mixture kept at the ordinary temperature for 24 hours; the alcohol is then partially evaporated on the water-

bath, the residue mixed with water and treated with a slight excess of dilute hydrochloric acid. The oil which is precipitated is extracted with ether, and after drying the extract over calcium chloride, the ether is evaporated. The dioxime remains in the form of a thick, yellowish oil which soon solidifies to a mass of crystals. After removing oily impurities by spreading the crystals on a porous plate, a nitrogen determination was made with the following result:—

0·1184 gram of substance gave 12 c.c. of nitrogen measured at 12° and 755 mm. pressure.

	Calculated for $C_{13}H_{26}N_2O_2$.	Found.
N	11·6 per cent.	11·9 per cent.

Diacetyldiethylpentanedioxime separates from a mixture of benzene and light petroleum in colourless, microscopic crystals melting at 110—111°. It is readily soluble in alcohol, ether, acetic acid, benzene, and other ordinary solvents, but only very sparingly in cold light petroleum; on adding light petroleum to the benzene solution, the dioxime is precipitated in a crystalline condition. It dissolves freely in alkalis and in moderately concentrated mineral acids.

Behaviour of Diacetyldiethylpentane with Concentrated Sulphuric Acid.

The chief object in view in preparing diacetyldiethylpentane was to study its behaviour with sulphuric acid. It has been shown in the previous paper that diacetylpentane dissolves in cold concentrated sulphuric acid, and is thereby converted into a compound $C_9H_{14}O$; the various theoretically possible formulæ for this compound have been already discussed, and it has been shown that its constitution is probably that of an orthomethyltetrahydrobenzene methyl ketone. One of the chief arguments in support of this view is the fact that diacetyldiethylpentane does not yield an analogous product under the same conditions, and is, in fact, unchanged by concentrated sulphuric acid.

About 8 grams of crude diacetyldiethylpentane was dissolved in about 60 grams of concentrated sulphuric acid; a slight development of heat was observed and the solution gradually turned brown. After keeping for about 24 hours, the solution was poured into a large volume of cold water and the precipitated oil extracted with ether. A yellowish-brown oil remained when the ether was evaporated, and the weight of this product was about 6·5 grams. The crude oil was submitted to fractional distillation under the ordinary pressure; the thermometer rose rapidly to 230°, and only a small quantity distilled between 230° and 240°, the greater portion passing over at 245—255°.

This fraction was collected separately, and analysed without any further purification. The following results were obtained:—

0·2228 gram of substance gave 0·5863 gram of CO_2 and 0·2239 gram of H_2O.

	Calculated for $C_{13}H_{22}O$.	Calculated for $C_{13}H_{24}O_2$.	Found.
C	80·4	73·6 per cent.	71·7 per cent.
H	11·3	11·3 „	11·2 „
O	11·3	15·1 „	17·1 „

This analysis shows that the fraction boiling at 245—255° consisted of impure diacetyldiethylpentane, and proves conclusively the absence of any compound richer in carbon. Since this fraction formed about 60 per cent. of the crude product, and most of the remainder boiled at a temperature above 255°, the experiment would show that the formation of a compound $C_{13}H_{22}O$ does not take place under these conditions.

In order to prove beyond doubt that such is really the case, the experiment was repeated in the following manner:—10 grams of almost pure diacetyldiethylpentane was dissolved in 300 grams of cold concentrated sulphuric acid and the solution kept for two days at the ordinary temperature; there was only a slight evolution of sulphurous anhydride, but the solution gradually darkened in colour. It was poured into a large volume of cold water, the oil extracted with ether, the extract dried over potassium carbonate and evaporated; the residual oil weighed about 8·8 grams. When the oil was distilled under the ordinary pressure, the thermometer rose at once to 215°, and the whole passed over between 215—270°, the greater portion boiling at about 250°. The fraction 215—270°, that is to say, the whole of the crude product, was distilled again under the ordinary pressure, and the portions passing over at 215—225° and 225—235° were collected separately. These two fractions were analysed with the following results:—

I. Fraction boiling at 215—225°: 0·1568 gram of substance gave 0·4141 gram of CO_2 and 0·1617 gram of H_2O.

II. Fraction boiling at 225—235°: 0·1654 gram of substance gave 0·4371 gram of CO_2 and 0·1733 gram of H_2O.

	Calculated for $C_{13}H_{22}O$.	Calculated for $C_{13}H_{24}O_2$.	Found. I.	Found. II.
C	80·4 p. c.	73·5 p. c.	72·06	72·5 p. c.
H	11·3 „	11·3 „	11·40	11·6 „
O	11·3 „	15·2 „	16·64	15·9 „

These analyses show that both fractions consisted of impure diacetyldiethylpentane, the purer of the two being naturally that of higher boiling point, as it approaches more closely that of the pure diketone. Now, since, if any dehydrating action had occurred, the resulting compound must have been contained in these two lowest boiling portions of the crude oil, it is clear that no compound of the composition $C_{13}H_{22}O$ had been formed.

This experiment, therefore, confirms the previous results and proves conclusively that diacetyldiethylpentane is not converted into a compound of the composition $C_{13}H_{22}O$ under conditions which, in the case of diacetylpentane, result in the formation of a compound of the composition $C_9H_{14}O$; this difference in behaviour can be explained only by assuming that the latter has the constitution of an orthomethyltetrahydrobenzene methyl ketone, a view which is fully borne out by other experiments.

ω-Acetyl-$\alpha\omega$-diethylcaproic Acid, $CH_3{\cdot}CO{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}COOH$.

The alkaline mother-liquors from which the diacetyldiethylpentane has been extracted with ether contain the potassium salts of acetyldiethylcaproic acid, acetic acid, and probably also diethylpimelic acid; these compounds having been produced by the hydrolysis of ethyl diacetyldiethylpimelate in accordance with the equations given on pp. 29 and 30. On acidifying with dilute sulphuric acid, a thick, yellowish oil is precipitated; the solution is shaken three or four times with ether, the ethereal extract dried over calcium chloride, and the ether evaporated. As the thick, sour-smelling oil which remained showed no signs of crystallising even when cooled below 0°, it was submitted to fractional distillation under reduced pressure (110 mm.). The acetic acid which passed over at the commencement of the distillation was readily identified by its odour and by converting it into ethyl acetate; the thermometer then rose rapidly to 200°, a small quantity only distilled below 240°, and the whole of the remainder passed over between 240° and 280°. The portion boiling at 240—280° was fractionated again under a pressure of 90 mm., and a fairly large quantity, boiling at 253—255°, collected separately.

The analysis of this fraction (b. p. 253—255°) showed that it consisted of acetyldiethylcaproic acid:

0·1420 gram of substance gave 0·3490 gram of CO_2 and 0·1305 gram of H_2O.

	Calculated for $C_{12}H_{22}O_3$.	Found.
C	67·28 per cent.	67·03 per cent.
H	10·28 ,,	10·21 ,,
O	22·43 ,,	22·76 ,,

Acetyldiethylcaproic acid is a thick, colourless liquid having an odour very like that of pyruvic acid; it becomes semi-solid when cooled strongly, but it has not yet been obtained in a crystalline condition. It is insoluble, or only very sparingly soluble, in water, but miscible with alcohol, ether, benzene, and other ordinary solvents in all proportions.

The *silver* salt, $CH_3{\cdot}CO{\cdot}CHEt{\cdot}(CH_2)_3{\cdot}CHEt{\cdot}COOAg$, was prepared by dissolving a portion of the fraction boiling at 253—255° in ammonia, and fractionally precipitating the neutral solution with silver nitrate. It is a colourless, seemingly amorphous compound, and rather sparingly soluble in hot water; it seems to be stable in the light.

A silver determination, made with a portion of the second fraction of the salt, gave the following result:—

0·4714 gram of substance gave 0·1605 gram of silver.

	Calculated for $C_{12}H_{21}O_3Ag$.	Found.
Ag	33·64 per cent.	34·03 per cent.

The first fraction gave a somewhat larger percentage of silver probably owing to the presence of small quantities of diethylpimelic acid.

In neutral aqueous solutions of the ammonium salt, lead acetate and mercuric chloride produce a colourless precipitate; ferric chloride, a buff-coloured precipitate; and copper sulphate, a dark-green precipitate.

The calcium salt and the barium salt are readily soluble in water.

ω-Acetyl-$\alpha\omega$-diethylcaproic Acid Oxime, $NOH{:}CMe{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}COOH$.

Acetyldiethylcaproic acid oxime can be obtained by treating the acid with hydroxylamine hydrochloride and excess of potash in dilute alcoholic solution; after keeping for about 24 hours, the alcohol is evaporated on the water-bath, the residue dissolved in water, the solution slightly acidified with hydrochloric acid, and extracted with ether. The crude product is a thick, yellowish oil, but it slowly solidifies to a mass of crystals; the crystalline substance, after having been spread on a porous plate and washed with a little light petroleum, melted at 102—103°.

A nitrogen determination gave the following result:—

0·0961 gram of substance gave 5·05 c.c. of nitrogen measured at 14° and 745 mm. pressure.

	Calculated for $C_{12}H_{23}NO_3$.	Found.
N.....	6·11 per cent.	6·12 per cent.

Acetyldiethylcaproic acid oxime crystallises from a mixture of benzene and light petroleum in colourless, microscopic plates; it is readily soluble in alcohol and benzene, but only sparingly in light petroleum, and, seemingly, insoluble in water; it dissolves freely in alkalis and in concentrated hydrochloric acid.

Heriott-Watt College, Edinburgh,
Chemical Laboratory.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, February*, 1890. Vol. LVII.]

ACTION OF DEHYDRATING AGENTS ON $\alpha\omega$-DIACETYLPENTANE. SYNTHESIS OF METHYLETHYLHEXAMETHYLENE.

By F. Stanley Kipping, Ph.D., D.Sc., and W. H. Perkin, Jun., Ph.D.

In a paper which we had the honour of communicating to the Society some time ago, we described the preparation and properties of $\alpha\omega$-diacetylpentane and of $\alpha\omega$-dibenzoylpentane, and stated also that our object in preparing these diketones was to study their behaviour with dehydrating and reducing agents.

It was thought possible that diketones of the constitution $R{\cdot}CO{\cdot}CH_2{\cdot}[CH_2]_n{\cdot}CH_2{\cdot}CO{\cdot}R$ might, under the influence of dehydrating agents, undergo internal condensation, and be converted into compounds having the constitution

$$\left.\begin{matrix} R{\cdot}C{:}C(CO{\cdot}R) \\ CH_2{\cdot}[CH_2]_n \end{matrix}\right\rangle,$$

a reaction which, to some extent, would be analogous to the formation of mesityl oxide from acetone.

The study of the action of reducing agents on diacetyl- and dibenzoyl-pentane also possessed great interest, as it was considered probable that in this manner dihydroxy-derivatives of the constitution

$$\begin{matrix} R{\cdot}C(OH)\text{——}C(OH){\cdot}R \\ CH_2{\cdot}[CH_2]_n{\cdot}CH_2 \end{matrix}$$

would be obtained. Both these reactions would, naturally, be controlled by the value of n.

Our views regarding the probable course of these reactions have been confirmed experimentally, and in the present paper we beg to lay before the Society the results which we have obtained in studying the action of dehydrating agents on diacetylpentane.

When diacetylpentane is treated with concentrated sulphuric acid, it is converted into a colourless liquid of the composition $C_9H_{14}O$.

$$C_9H_{16}O_2 - H_2O = C_9H_{14}O.$$

Considerable difficulty has been experienced in determining the constitution of this interesting substance, as, in accordance with the present views on the structure of organic compounds, a substance derived from diacetylpentane by the elimination of one molecule of water might be represented by any one of the following constitutional formulæ:—

I. $CH_3{\cdot}C{:}C{\cdot}[CH_2]_4{\cdot}CO{\cdot}CH_3$ II. $CH{:}C{\cdot}[CH_2]_5{\cdot}CO{\cdot}CH_3$

III. $CH_2{:}C{:}CH{\cdot}[CH_2]_4{\cdot}CO{\cdot}CH_3$ IV. $CH_3{\cdot}C(-O-)C{\cdot}CH_3$ with $CH{\cdot}[CH_2]_3{\cdot}CH$

V. $CH_3{\cdot}C(=CH-[CH_2]_3>)CH(CO{\cdot}CH_3)$ VI. $CH_2{:}C(-CH_2-[CH_2]_3>)CH(CO{\cdot}CH_3)$

VII. $CH_3{\cdot}C(=CH{\cdot}CO)CH_2{\cdot}[CH_2]_3{\cdot}CH_2$ VIII. $CH_3{\cdot}C{:}C(CO{\cdot}CH_3)<CH_2-[CH_2]_3>$

IX. $CH_3{\cdot}C(=C{\cdot}[CH_2]_{n'}{\cdot}CO{\cdot}CH_3)\llcorner[CH_2]_n\lrcorner$ $(n = 1, 2, \text{or } 3)$ $(n' = 3, 2, \text{or } 1)$

The results of experiments which bear directly on the question of the constitution of this compound $C_9H_{14}O$, briefly stated, are the following:—

It undergoes no change when treated with 80 per cent. sulphuric acid, or when heated with a concentrated solution of mercuric chloride.

It is not acted on by phosphoric anhydride in ethereal solution.

It combines readily with hydroxylamine, yielding an oxime, $C_9H_{15}NO$, and with phenylhydrazine, forming a hydrazone, $C_{15}H_{20}N_2$.

When treated with sodium in moist ethereal solution, it combines directly with 4 atoms of hydrogen, and is converted into an alcohol, $C_9H_{18}O$.

The iodide from this alcohol is reduced when it is heated with fuming hydriodic acid and amorphous phosphorus, yielding a hydrocarbon, C_9H_{18}.

αω-Diacetyl-*αω*-diethylpentane, $COMe{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}COMe$, is not acted on by cold concentrated sulphuric acid.

αω-Dibenzoylpentane, $COPh{\cdot}[CH_2]_5{\cdot}COPh$, when warmed with phosphoric anhydride, is converted into a compound of the composition $C_{19}H_{16}O$.

From these facts, the constitution of the compound $C_9H_{14}O$ may be argued with a considerable degree of certainty. Its negative behaviour with 80 per cent. sulphuric acid and with mercuric chloride is strong evidence against the constitution I or II, because substances of this nature (derivatives of acetylene), under the same conditions as those employed, almost invariably combine with 1 mol. of water, and are converted into saturated compounds.

The fact that the compound $C_9H_{14}O$ is not acted on by phosphoric anhydride goes to show that the first three formulæ are all improbable, as a compound possessing the constitution I, II, or III would probably be converted into an unsaturated hydrocarbon C_9H_{12}.

The formation of the oxime and the hydrazone shows that it is a ketone, and cannot have the constitution represented by formula IV.

A conclusive proof of the inadmissibility of the formulæ I, II, III, and IV is afforded by the behaviour of the compound $C_9H_{14}O$ on reduction; when treated with sodium in moist ethereal solution, and subsequently with fuming hydriodic acid, it is converted into a hydrocarbon C_9H_{18}, whereas a substance represented by any one of these four formulæ would yield a normal paraffin C_9H_{20}.

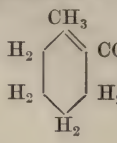
It is, therefore, an easy task to prove conclusively that the constitution of the compound $C_9H_{14}O$ is not represented by any of the first four formulæ, but it is much more difficult to distinguish between the remaining five.

A compound having the constitution shown in V, VI, VII, VIII, or IX would be expected to behave in most respects like the substance $C_9H_{14}O$, that is, to give an oxime and a hydrazone, to yield an alcohol $C_9H_{18}O$ on reduction, and when heated with hydriodic acid to be converted into a hydrocarbon C_9H_{18}.

The behaviour of $\alpha\omega$-diacetyl-$\alpha\omega$-diethylpentane with sulphuric acid affords, however, a means of deciding between these formulæ. An examination of the formulæ V to IX shows clearly that the presence of a methylene-group in direct combination with the carbonyl-group is necessary to the formation of the compound $C_9H_{14}O$, only if it possesses the constitution shown in VIII; if, on the other hand, it had the constitution V, VI, VII, or IX, its formation could take place if one of the hydrogen-atoms in both these methylene-groups were replaced by a radicle such as ethyl, or in other words, diacetyldiethylpentane, $COMe{\cdot}CHEt{\cdot}[CH_2]_3{\cdot}CHEt{\cdot}COMe$, should give a condensation-product when treated with sulphuric acid just as readily as diacetylpentane.

Supposing, for example, that the formula VII represents the constitution of the compound $C_9H_{14}O$, diacetyldiethylpentane should yield an analogous condensation-product of the constitution

$$CH_3{\cdot}C{=}\!=\!=\!=\!=CH{\cdot}CO$$
$$\quad\quad\quad

stitution of the compound $C_9H_{14}O$ is represented by formula VIII, and that it is Δ^1-orthomethylacetyltetrahydrobenzene,*  ,

(Δ^1-orthomethyltetrahydrobenzene methyl ketone).

Dibenzoylpentane, $COPh\cdot[CH_2]_5\cdot COPh$, when warmed with phos phoric anhydride, is readily converted into a compound $C_{19}H_{18}O$; if, as is probable, this compound should, on further investigation, prove to have a constitution analogous to that of the condensation-product of diacetylpentane, this fact would be additional evidence in favour of our views regarding the mechanism of these internal condensations by proving the inadmissibility of the formulæ II, III, VI, and VII. As we are at present engaged in examining this compound, and in investigating the behaviour of dibenzoylpentane with reducing agents, we hope to be able to communicate the results to the Society at an early date.

Orthomethyltetrahydrobenzene Methyl Ketone,

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot COMe.$$

Orthomethyltetrahydrobenzene methyl ketone (orthomethylacetyl-tetrahydrobenzene) is formed by the action of dehydrating agents on *aω*-diacetylpentane; it is best prepared by dissolving the diketone in concentrated sulphuric acid.

Diacetylpentane (not more than 30 grams) is added in small portions at a time to six or eight times its volume of concentrated sulphuric acid; as considerable evolution of heat occurs, the solution is cooled under the tap after each addition of the diketone, otherwise the yield is decreased. The resulting solution, which varies in colour from brownish-red to dark brown, is kept in a loosely-stoppered flask at the ordinary temperature from one to two days, during which time it darkens in colour, and a slight evolution of sulphurous anhydride occurs. The solution is then poured into a large volume of cold water, the greenish-yellow oil which is precipitated is extracted by shaking two or three times with ether, and the ethereal extract, after having been dried over potassium carbonate, is evaporated. A yellow, mobile oil, smelling strongly of peppermint, is obtained; the yield of the crude product is, on the average, 85—90 per cent. of the diketone employed. When this oil is distilled under the ordinary pressure, a small quantity passes over between 120° and 190°, but the principal

* Compare Baeyer, "Ueber die Constitution des Benzols" (*Annalen*, **245**. 111).

portion distils between 190° and 210°; if the distillation is discontinued as soon as the thermometer rises above 210—215°, a small quantity of a thick, brown oil, which will be referred to below, remains in the flask.

The fraction 190—210° still contains traces of unchanged diketone; pure orthomethyltetrahydrobenzene methyl ketone, boiling constantly at 205—206°, can only be obtained by again treating this product with sulphuric acid and fractionating two or three times under the ordinary pressure. The analysis gave the following results:—

0·1855 gram of substance gave 0·5294 gram CO_2 and 0·1720 gram H_2O.

	Calculated for $C_9H_{14}O$.	Found.
C	78·26 per cent.	77·84 per cent.
H	10·14 „	10·30 „
O	11·60 „	11·86 „

Orthomethyltetrahydrobenzene methyl ketone is a colourless, mobile oil with a strong odour of peppermint, and a sharp, somewhat bitter taste. It boils at 205—206° (about 755 mm.) without decomposition, and is readily volatile with steam. It is insoluble in and specifically lighter than water, but it is miscible with the ordinary organic solvents in all proportions. It does not combine with sodium hydrogen sulphite even when kept for a long time with a saturated aqueous solution of the salt, but it combines readily with hydroxylamine. When treated with excess of sodium in moist ethereal solution, it is converted into orthomethylhexamethylene methyl carbinol.

In order to determine the constitution of this compound, $C_9H_{14}O$, it was necessary, in the first place, to ascertain whether it contained a "treble linking;" the following experiments were made with this object:—

A small quantity of the pure compound was dissolved in 80 per cent. sulphuric acid, and the solution kept for a few days at the ordinary temperature; it was then diluted with water, warmed for about half an hour on the water-bath, and after adding a large volume of water, extracted with ether. The boiling point and other properties of the oil which was obtained showed that it consisted entirely of the original substance, no reaction having taken place.

About 4 grams of the pure compound was mixed with a warm, concentrated, aqueous solution of mercuric chloride, and the mixture heated at 95—98° for three hours with constant shaking. A small quantity of the mercuric salt seemed to be reduced, but otherwise no reaction was observed. The mixture was then warmed with a little

concentrated hydrochloric acid, the oil extracted with ether, and distilled. The whole passed over within a range of a few degrees, and consisted of the original substance.

These experiments having shown that the compound $C_9H_{14}O$ does not combine with 1 mol. of water when submitted to the treatment usually employed in the case of substances containing trebly-bound carbon-atoms, it seemed interesting to ascertain, whether, under the influence of dehydrating agents more powerful than concentrated sulphuric acid, it would be converted into a hydrocarbon C_9H_{12}. The formation of such a compound would have shown that the original oil was most probably an open-chain derivative of the constitution given in one of the first three formulæ (see p. 14).

About 10 grams of the pure ketone was dissolved in about 100 c.c. of pure, dry ether, and a considerable quantity of phosphoric anhydride added to the solution; no reaction was observed even after keeping for about 24 hours at the ordinary temperature. The ethereal solution was filtered and evaporated, and the residual oil distilled under the ordinary pressure. It commenced to boil at about 193°, and almost the whole passed over between 203 and 206°, traces of a thick, yellowish oil, probably a condensation-product, remaining in the flask. The fraction 203—206° consisted of unchanged ketone, as was shown by its boiling point and other properties.

Action of Hydroxylamine and of Phenylhydrazine on Orthomethyltetrahydrobenzene Methyl Ketone.

The compound produced by the action of sulphuric acid on $\alpha\omega$-diacetylpentane combines readily with hydroxylamine, yielding a colourless monoxime; it also forms a hydrazone-derivative when it is heated with phenylhydrazine.

Orthomethyltetrahydrobenzene Methyl Ketone-oxime,

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot CMe{:}N\cdot OH.$$

Orthomethyltetrahydrobenzene methyl ketone-oxime is best prepared by treating the ketone with hydroxylamine by Auwers' method. About 15 grams of potash are dissolved in dilute alcohol, 5 grams of hydroxylamine hydrochloride added to the solution, and 10 grams of the ketone poured into the mixture. After being kept for about 24 hours, the whole is warmed gently on the water-bath until most of the alcohol has evaporated; it is then cooled, diluted with water, and slightly acidified with dilute hydrochloric acid. The yellowish oil which is precipitated is extracted with ether, the ethereal extract dried over calcium chloride, and evaporated.

The oxime remains as a yellowish oil which, after being kept over sulphuric acid under reduced pressure, is obtained in an almost pure condition, as is shown by the following analyses made with different samples of the crude product:—

I. 0·1640 gram gave 13·6 c.c. of nitrogen measured at 742 mm. and 20°.

II. 0·1560 gram gave 12·3 c.c. of nitrogen measured at 740 mm. and 20°.

	Calculated for $C_9H_{15}NO$.	Found. I.	Found. II.
N.....	9·15 per cent.	9·23	8·86 per cent.

It is a thick, yellowish liquid, with a rather pleasant odour, and shows no signs of crystallising even when kept for a long time over sulphuric acid. It is insoluble or very sparingly soluble in cold, and only very slightly soluble in warm water, but it dissolves freely in potash and concentrated mineral acids, and it is miscible with alcohol, ether, &c., in all proportions. It dissolves in concentrated sulphuric acid with development of heat, yielding a clear yellow solution; on adding alkali to the diluted solution, no oil is precipitated, but on boiling the alkaline solution ammonia is evolved. It cannot be distilled under the ordinary pressure, as when heated, even in small quantities, it is completely decomposed.

Beckmann (*Berichte*, **20**, 2580) has shown that some oximes, under the influence of acetic chloride, glacial acetic acid, &c., undergo an intramolecular change, the group of atoms C.N·OH being converted into CO·NH; the compounds thus produced are readily decomposed on hydrolysis into an amine and an acid.

Considerable quantities of the oxime of orthomethyltetrahydrobenzene methyl ketone were prepared in order to study its behaviour with Beckmann's reagents, as it was thought that in this way the constitution of the ketone might be ascertained.

For this purpose, 7 grams of the oxime was dissolved in 70 grams of glacial acetic acid and 14 grams of acetic anhydride, and the mixture, after having been saturated in the cold with hydrogen chloride, was heated at 100° for four or five hours in sealed tubes. At the end of this time, the solution had turned dark reddish-brown, but no separation of crystals occurred. On neutralising with sodium carbonate, a strong basic odour was perceptible, and a brownish-black oil separated at the surface of the solution. The oil was extracted with ether, and the ethereal extract dried and evaporated, when 5 grams of a dark-coloured oil remained; this was insoluble in water and in cold hydrochloric acid, but when heated with hydrochloric

acid it was almost completely decomposed, yielding large quantities of resinous products and a small quantity of a yellow neutral oil which was not investigated very closely.

The sodium carbonate solution from which the oil had been extracted was rendered strongly alkaline with potash, and boiled for two hours, the distillate being collected in dilute hydrochloric acid. On adding platinic chloride to the dilute acid solution, a precipitate was produced, but this precipitate consisted of pure ammonium platinochloride, as was shown by its characteristic crystalline form, and also by the following analysis:—

0·3865 gram of the platinochloride gave 0·1694 gram of platinum.

	Calculated for $(NH_3)_2H_2PtCl_6$.	Found.
Pt.....	43·9 per cent.	43·83 per cent.

The experiment was repeated under similar conditions, but with the same results; a small quantity of a neutral oil was obtained, and the only basic product which could be isolated was ammonia.

When the oxime is treated with acetic chloride at the ordinary temperature, an extremely violent reaction occurs, and a dark-red solution is obtained. If the excess of acetic chloride is evaporated, and the residue is heated for a long time on the water-bath, it darkens in colour, and finally becomes black and very thick. A small quantity of a colourless crystalline compound can be isolated from this residue; this substance is insoluble in water, and only very sparingly soluble in ether; it does not give any basic odour when boiled with potash. It was not investigated, owing to the very small quantity at our disposal.

Orthomethyltetrahydrobenzene Methyl Ketone-hydrazone,

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot CMe{:}N_2HPh.$$

The hydrazone-derivative of the ketone is best prepared by heating pure orthomethyltetrahydrobenzene methyl ketone with a slight excess of phenylhydrazine for two to three hours on the water-bath. The product is purified by dissolving it in ether, and washing the ethereal solution with dilute hydrochloric acid until it is free from phenylhydrazine. The solution is then dried over calcium chloride, the ether evaporated, and the residue kept for 24 hours over sulphuric acid under reduced pressure.

The analysis gave the following results:—

0·2218 gram of substance gave 24·95 c.c. of nitrogen measured at 18° and 740 mm.

	Calculated for $C_{15}H_{20}N_2$.	Found.
N	12·3 per cent.	12·3 per cent.

It is a thick, yellowish-brown oil, which shows no signs of crystallising; when left exposed to the air it gradually darkens in colour, and decomposes with evolution of gas. It is insoluble or only very sparingly soluble in water, but readily soluble in alcohol and ether.

Reduction of Orthomethyltetrahydrobenzene Methyl Ketone.

Methyltetrahydrobenzene methyl ketone yields three compounds when it is reduced with sodium in moist ethereal solution. When a large excess of sodium is employed, it is converted principally into orthomethylhexamethylene methyl carbinol, small quantities of a condensation-product being also formed. If only a slight excess of sodium is used, orthomethyltetrahydrobenzene methyl carbinol seems to be the principal product of the reaction.

Methylhexamethylene Methyl Carbinol,

$$CH_2<\begin{matrix}CH_2\cdot CHMe\\ CH_2-CH_2\end{matrix}>CH\cdot CHMe\cdot OH.$$

Orthomethylhexamethylene methyl carbinol is prepared by treating pure methyltetrahydrobenzene methyl ketone with sodium in moist ethereal solution. The ketone is dissolved in about twenty times its volume of pure ether, the solution placed in a large bottle containing about 60 c.c. of water and provided with a reflux condenser, and small quantities of sodium are introduced from time to time. As soon as about 20 times the quantity of sodium theoretically necessary for complete reduction has been added, the ethereal solution is separated, and the residue extracted twice with ether. The ethereal solutions are mixed together, dried over potassium carbonate, filtered, and evaporated. A moderately thick, slightly yellow oil remains, the quantity of which is approximately equal to that of the ketone employed. On distilling it under 40 mm. pressure, the thermometer rises rapidly to 120°, and between this temperature and 280° the whole passes over. The fraction 120—280° is now repeatedly refractionated under reduced pressure (40 mm.), and is thus separated into a portion boiling at 127—137°, which consists of slightly impure methylhexamethylene methyl carbinol, and a portion boiling at about 250—260°. The higher boiling compound is only formed in comparatively small quantities, and will be again referred to.

The principal fraction, boiling at 127—137° (40 mm.), is again

submitted to fractional distillation under reduced pressure, and finally under the ordinary pressure, the methylhexamethylene methyl carbinol being thus obtained in a pure state.

The analyses gave the following results:—

I. 0·1160 gram of substance gave 0·3221 gram of CO_2 and 0·1315 gram of H_2O.

II. 0·1494 gram of substance gave 0·4150 gram of CO_2 and 0·1685 gram of H_2O.

	Calculated for $C_9H_{18}O$.	Found. I.	Found. II.
C	76·06 per cent.	75·71	75·72 per cent.
H	12·66 „	12·59	12·53 „
O	11·27 „	11·70	11·75 „

Methylhexamethylene methyl carbinol is a thick, colourless oil with a smell very like that of menthol; it boils at 195—200° under the ordinary atmospheric pressure, and at 130—133° at 40 mm. without decomposition. It is only sparingly soluble in water, but miscible with alcohol, ether, &c., in all proportions. It dissolves in concentrated hydriodic acid with development of heat, and in a very short time the iodide separates from the solution.

Methylhexamethylene Methyl Carbinyl Acetate,

$$CH_3{\cdot}COO{\cdot}CHMe{\cdot}CH<\begin{matrix}CHMe{\cdot}CH_2\\ CH_2-CH_2\end{matrix}>CH_2.$$

Methylhexamethylene methyl carbinyl acetate is formed by treating methylhexamethylene methyl carbinol with acetic anhydride. The pure alcohol is boiled for 2 to 3 hours with excess of acetic anhydride in a flask provided with a reflux condenser; the excess of anhydride is then distilled off, and the residue is fractionated under the ordinary pressure. The thermometer rises rapidly to about 195°, almost the whole distilling between 200 and 210°. By fractionating the distillate two or three times, the acetate is obtained in a pure condition, as is shown by the following analysis:—

0·1541 gram of substance gave 0·4058 gram of CO_2 and 0·1567 gram of water.

	Calculated for $C_{11}H_{20}O_2$.	Found.
C	71·74 per cent.	71·75 per cent.
H	10·87 „	11·29 „
O	17·38 „	16·96 „

It is a colourless, mobile oil with a sweet rather pleasant odour,

and boils at 204—208° under the ordinary pressure without decomposition. It is seemingly insoluble or only very sparingly soluble in water, but it is miscible with ether, alcohol, &c., in all proportions. When boiled with alcoholic potash, it is readily hydrolysed, being reconverted into the alcohol.

α-Iodoethylmethylhexamethylene, $CH_2<\begin{matrix}CH_2\cdot CHMe\\CH_2-CH_2\end{matrix}>CH\cdot CHMeI$.

Methylhexamethylene methyl carbinol dissolves in concentrated hydriodic acid, a considerable rise of temperature taking place, and after a very short time the iodide separates from the solution in the form of an oil. This compound is best prepared by heating the alcohol with excess of concentrated hydriodic acid (sp. gr. 1·96) at 180° in a sealed tube for about 4 hours. After diluting with water, the precipitated iodide is extracted with ether, the solution washed, first with water and then with very dilute sodium carbonate solution, until free from acid, then dried over calcium chloride, and evaporated. The residual oil can be easily obtained in a pure condition by submitting it to fractional distillation under reduced pressure.

An iodine determination by Carius' method gave the following result :—

0·2420 gram of substance gave 0·2270 gram of silver iodide.

	Calculated for $C_9H_{17}I$.	Found.
I	50·29 per cent.	50·68 per cent.

Iodoethylmethylhexamethylene is a colourless mobile oil with an odour very like that of the iodides of the higher normal alcohols. It boils at 178–180° (110 mm.), seemingly without decomposition, and is insoluble in water, but readily soluble in the ordinary neutral organic solvents. It rapidly darkens on exposure to light.

The fraction boiling at 240—260° (40 mm.), obtained in small quantities in the preparation of methylhexamethylene methyl carbinol, was distilled again under reduced pressure (50 mm.), and the portion passing over between 255—265° was collected separately. The analysis of this product gave results agreeing with the composition $C_{18}H_{32}O_2$.

0·2366 gram of substance gave 0·6655 gram of CO_2 and 0·2454 gram of H_2O.

	Calculated for $C_{18}H_{32}O_2$.	Found.
C	77·14 per cent.	76·70 per cent.
H.....	11·43 „	11·52 „

It is a very thick, yellowish oil with a peculiar aromatic odour, insoluble in water but miscible with alcohol, ether, &c., in all proportions.

No experiments have yet been made to ascertain the constitution of this compound, but it is most probably formed by the condensation of 1 mol. of orthomethyltetrahydrobenzene methyl ketone with 1 mol. of methylhexamethylene methyl ketone in a manner somewhat analogous to that in which pinacone is formed by the reduction of acetone, so that its constitution may be expressed by the formula—

$$CH_2<\begin{matrix}CH_2\cdot CHMe\\CH_2-CH_2\end{matrix}>CH\cdot CMe(OH)\cdot CMe(OH)\cdot C<\begin{matrix}CMe\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>CH_2.$$

Methyltetrahydrobenzene Methyl Carbinol,

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot CHMe\cdot OH.$$

Orthomethyltetrahydrobenzene methyl carbinol is formed, as has been already stated, together with methylhexamethylene methyl carbinol when the ketone is reduced with a slight excess of the theoretical quantity of sodium in moist ethereal solution. It is obtained as follows:—Methyltetrahydrobenzene methyl ketone is dissolved in pure ether and treated with sodium under the conditions described in the preparation of the hexamethylene compound. After adding a little more sodium than is theoretically necessary, the ethereal solution is separated, dried over potassium carbonate, and evaporated. When the residual oil is carefully and repeatedly fractionated under reduced pressure (50 mm.), it is separated into two portions, the principal fraction, boiling at 141—143°, consisting of methyltetrahydrobenzene methyl carbinol, mixed possibly with small quantities of the hexamethylene-derivative and unchanged ketone.

It is a colourless, mobile oil, boils at 141—143° (50 mm.), and resembles methylhexamethylene methyl carbinol in its behaviour with solvents.

The following results were obtained on analysis:—

0·1599 gram of substance gave 0·4509 gram of CO_2 and 0·1703 gram of H_2O.

	Calculated for $C_9H_{16}O$.	Found.
C	77·14 per cent.	76·90 per cent.
H	11·43 „	11·83 „
O	11·43 „	11·27 „

Reduction of Methylhexamethylene Methyl Carbinol.

Orthomethylethylhexamethylene, $CH_2<\begin{matrix}CH_2\cdot CHMe\\CH_2-CH_2\end{matrix}>CHEt$.

Orthomethylethylhexamethylene is the final product of the reduction of methyltetrahydrobenzene methyl ketone, and is obtained when methylhexamethylene methyl carbinol is reduced with hydriodic acid.

Its preparation is carried out as follows:—About 12 grams of the pure alcohol is heated with excess of fuming hydriodic acid for 2–3 hours in a flask provided with a reflux condenser, and, after diluting with water, the precipitated iodide is extracted with ether. The crude iodide, in quantities of about 3 grams, is heated in a sealed tube at 230—240° for 8 hours with a large excess of hydriodic acid of sp. gr. 1·96 and a little amorphous phosphorus. There is great pressure in the tube when cold, and the hydrocarbon forms a layer on the surface of the acid; this is separated from the acid, dried over potassium carbonate, and distilled. The thermometer rises rapidly to 120°, and the whole distils between 120 and 160°. The crude product is then repeatedly fractionated over sodium and finally over potassium. The hydrocarbon is thus obtained in a pure state and on analysis gave the following results:—

I. 0·1211 gram of substance gave 0·3795 gram of CO_2 and 0·1590 gram of H_2O.

II. 0·1100 gram of substance gave 0·3450 gram of CO_2 and 0·1434 gram of H_2O.

	Calculated for C_9H_{18}.	Found. I.	Found. II.
C	85·7 per cent.	85·47	85·54 per cent.
H.....	14·3 „	14·58	14·47 „

A vapour-density determination made by Hofmann's method in the vapour of aniline gave the following results:—

0·0502 gram of substance yielded 57·0 c.c. of vapour. Temperature of vapour 184°. Bar. 765 mm. Difference of level 582 mm. Temperature of air 15°.

	Calculated for C_9H_{18}.	Found.
Molecular weight	126	125

Orthomethylethylhexamethylene is a colourless, very mobile oil, the odour of which cannot be distinguished from that of the liquid paraffins. It boils at 150—152° and is insoluble in water and concentrated hydriodic acid, but miscible with ether, alcohol, &c., in all pro-

portions. When treated with cold concentrated nitric acid, oxidation quickly commences and the mixture becomes very hot. A small quantity of the hydrocarbon was treated with nitric acid in the cold; as soon as the first energetic reaction was at an end, the mixture was heated on the water-bath in a flask provided with a reflux condenser. The hydrocarbon gradually disappeared, dense, brown fumes being evolved, and finally a homogeneous liquid was obtained. The solution remained clear on adding water, and on evaporation it yielded only a very small quantity of a thick, syrupy residue which was not investigated owing to the small amount of material at our disposal.

Condensation-products of αω-Diacetylpentane.

A small quantity of two condensation-products are obtained in the preparation of diacetylpentane by the hydrolysis of ethyl diacetylcaproate (Trans., 1889, **55**, 333); these products remain in the form of a thick brown oil when the crude diacetylpentane is distilled under reduced pressure. The residues obtained in this way from several operations were mixed together and submitted to fractional distillation under a pressure of 35 mm. The thermometer rose rapidly to about 230°, and between about 250 and 280° a considerable proportion of the oil distilled; the temperature then rose quickly to 310°, the remainder passing over between 310° and 340°.

The portion collected between 250 and 280° was fractionated two or three times under the same pressure, and in this way a yellow oil boiling at 265—275° was obtained.

The analysis of this compound gave the following results:—

I. 0·1418 gram substance gave 0·4030 gram of CO_2 and 0·1329 gram of H_2O.

II. 0·1118 gram of substance gave 0·3190 gram of CO_2 and 0·1047 gram of H_2O.

	Calculated for $C_{18}H_{28}O_2$.	Found. I.	Found. II.
C	78·26 per cent.	77·82	77·70 per cent.
H	10·14 „	10·40	10·30 „
O	11·60 „	11·78	12·00 „

A molecular weight determination was carried out by Raoult's method in glacial acetic acid solution and resulted as follows:—

Freezing point of the acetic acid 15·740°.

1·4882 gram of substance dissolved in 67·25 grams of acetic acid lowers the freezing point 0·30°.

	Calculated for $C_{18}H_{28}O_2$.	Found.
Molecular weight	276	287

These results show that this condensation product is formed by the combination of 2 mols. of diacetylpentane with elimination of 2 mols. of water; as the diketone is readily converted into methyltetrahydrobenzene methyl ketone with elimination of 1 mol. of water, the constitution of the compound $C_{18}H_{28}O_2$ is most probably expressed by the formula—

$$CH_2<\begin{matrix}CH_2\cdot CMe\\CH_2\cdot CH_2\end{matrix}>C\cdot CMe:CH\cdot CO\cdot[CH_2]_5\cdot COMe.$$

It is a yellowish, very thick oil, boiling at 265—275° (35 mm.) seemingly without decomposition, and it shows no signs of crystallising even when kept for a long time in a desiccator under reduced pressure. It is miscible with alcohol, ether and other neutral solvents in all proportions, but it is insoluble in water.

The other fraction, boiling at 310—340° (35 mm.), which is obtained from the residues in the preparation of diacetylpentane was likewise submitted to fractional distillation, and in this way a yellow oil boiling at 320—330° can be isolated without much difficulty.

This compound gave the following results on analysis :—

0·1988 gram of substance gave 0·5702 gram of CO_2 and 0·1828 gram of H_2O.

	Calculated for $C_{27}H_{42}O_3$.	Found.
C	78·26 per cent.	78·22 per cent.
H.....	10·14 „	10·20 „
O	11·60 „	11·58 „

It is a yellow oil with a slight aromatic odour, and resembles the preceding compound in its behaviour with solvents; it is of an almost syrupy consistency, but shows no signs of crystallising when kept for a long time in a desiccator under reduced pressure.

The higher boiling point of this compound indicates a more complicated constitution than that of the condensation-product described above, and it is probably formed by the combination of 3 mols. of diacetylpentane, with elimination of 3 mols. of water, according to the equation, $3C_9H_{16}O_2 = C_{27}H_{42}O_3 + 3H_2O$.

Action of Dehydrating Agents on αω-Dibenzoylpentane.

The investigation of the behaviour of dibenzoylpentane with dehydrating and reducing agents has been commenced and has already

led to interesting results, but the compounds obtained have not yet been examined very fully. A very short account of some of our experiments may, however, be suitably given in this paper on account of their bearing on the question of the constitution of methyltetrahydrobenzene methyl ketone.

Concentrated sulphuric acid seems to have no dehydrating action on dibenzoylpentane in the cold, as is shown by the following experiment. About 0·5 gram of the pure diketone was dissolved in concentrated sulphuric acid, and the solution kept at the ordinary temperature for three days; it gradually became violet in colour and a small quantity of sulphurous anhydride was evolved. The addition of water caused the precipitation of a colourless compound, which, after recrystallisation from dilute methyl alcohol, melted at 66—67°, and was found to consist of unchanged dibenzoylpentane; the quantity obtained was about 0·46 gram.

When dibenzoylpentane is warmed with phosphoric anhydride it is converted into a compound having the composition $C_{19}H_{18}O$, but considerable quantities of resinous products are also formed.

The compound $C_{19}H_{18}O$ crystallises from alcohol in beautiful, colourless needles, melting at 110—111°.

An analysis gave the following results:—

0·1187 gram of substance gave 0·3787 gram of CO_2 and 0·0744 gram of H_2O.

	Calculated for $C_{19}H_{18}O$.	Found.
C	87·02 per cent.	86·84 per cent.
H	6·87 „	6·96 „
O	6·11 „	6·20 „

This substance is at present under investigation, and will form the subject of a paper which we hope soon to be able to communicate to the Society.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

ACTION OF REDUCING AGENTS ON $\alpha\alpha'$-DIACETYLPENTANE. SYNTHESIS OF DIMETHYLDIHYDROXYHEPTAMETHYLENE

By F. Stanley Kipping, Ph.D., D.Sc., and W. H. Perkin, Junr., Ph.D., F.R.S.

$\alpha\alpha'$-Diacetylpentane, a diketone which has the constitution

$$COMe\cdot[CH_2]_5\cdot COMe,$$

as is proved by its method of preparation and properties (compare Trans., 1889, **55**, 330), behaves in a most remarkable manner both with dehydrating and with reducing agents.

When treated with concentrated sulphuric acid under suitable conditions, it is converted into a compound of the composition $C_9H_{14}O$, which, as has been previously shown (Trans., 1890, **57**, 13), is, doubtless, a methylacetyltetrahydrobenzene of the constitution

$$CH_2\begin{<}{CH_2\cdot CMe \atop CH_2\cdot CH_2}\end{>}C\cdot COMe.$$

On reduction with sodium in moist ethereal solution, $\alpha\alpha'$-diacetylpentane yields as principal product a colourless liquid of the composition $C_9H_{18}O_2$; the formation of this compound is represented by the equation

$$C_9H_{16}O_2 + H_2 = C_9H_{18}O_2.$$

The method of preparation, properties, and some derivatives of this reduction product are described in the present paper, as are also various experiments which were made with the object of ascertaining its constitution; the results of these experiments seem to prove satisfactorily that the compound in question is a dimethyldihydroxyheptamethylene of the constitution

$$CH_2\begin{<}{CH_2\cdot CH_2\cdot CMe\cdot OH \atop CH_2\cdot CH_2\cdot CMe\cdot OH}\end{>}.$$

The formation of a heptamethylene derivative in this simple manner is an extremely interesting reaction, which may be regarded as analogous to the production of pinacone from acetone; the only difference between the two reactions is that in the formation of pinacone, combination takes place between two carbon atoms of two different acetone molecules, yielding an open-chain compound, whereas in the case of dimethyldihydroxyheptamethylene a closed-chain derivative is formed by the union of two carbon atoms of one and the same molecule of diacetylpentane.

The analogy between the two reactions is clearly shown with the aid of the following equations:—

$$\begin{matrix}(CH_3)_2CO\\(CH_3)_2CO\end{matrix} + H_2 = \begin{matrix}(CH_3)_2C\cdot OH\\|\\(CH_3)_2C\cdot OH\end{matrix}.$$

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot C(CH_3)O\\CH_2\cdot CH_2\cdot C(CH_3)O\end{matrix} + H_2 = CH_2<\begin{matrix}CH_2\cdot CH_2\cdot C(CH_3)\cdot OH\\|\\CH_2\cdot CH_2\cdot C(CH_3)\cdot OH\end{matrix}.$$

Constitution of the Reduction Product of αα′-Diacetylpentane.

In endeavouring to assign the correct constitutional formula to the reduction product of diacetylpentane, it is, in the first place, important to notice that the compound in question is formed by the addition of only two atoms of hydrogen to the diketone, a fact which is conclusively proved by the results of twelve analyses. Although many different samples have been analysed, the quantity of hydrogen found was never more than 11·75 per cent., usually about 11·5 per cent., results which agree very closely with those required for a compound of the composition $C_9H_{16}O_2$, which contains 11·39 per cent. of hydrogen.

A compound of the constitution $OH\cdot CHMe\cdot[CH_2]_5\cdot CHMe\cdot OH$ which, it might be expected, would be produced by the reduction of the diketone, is evidently not formed in any appreciable quantity under the conditions employed in our experiments, as such a compound would contain 12·5 per cent. of hydrogen.

Now a compound of the composition $C_9H_{18}O_2$, obtained by reducing αα′-diacetylpentane, $COMe\cdot[CH_2]_5\cdot COMe$, may, theoretically, have the constitution represented by one of the following formulæ:—

I.

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot COMe\\CH_2\cdot CH_2\cdot CHMe\cdot OH\end{matrix}.$$

II.

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMe\cdot OH\\|\\CH_2\cdot CH_2\cdot CMe\cdot OH\end{matrix}.$$

If its constitution be expressed by formula I, it would, in all probability, show the following behaviour:—

1. It would combine with hydroxylamine to form an oxime of the constitution $OH{\cdot}N{:}CMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}OH$, and with phenylhydrazine to form a hydrazone of the composition $C_9H_{18}O{:}N_2HPh$.

2. It would be converted into a monacetyl-derivative of the constitution $COMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}OAc$, on treatment with acetic anhydride.

3. When treated with hydrobromic acid, a monobromo-derivative of the constitution $COMe{\cdot}[CH_2]_5{\cdot}CHMeBr$ would be produced, whereas phosphorus pentabromide would convert it into a tribromide of the constitution $CMeBr_2{\cdot}[CH_2]_5{\cdot}CHMeBr$.

4. It would be easily reduced to a dihydric alcohol of the constitution $OH{\cdot}CHMe{\cdot}[CH_2]_5{\cdot}CHMe{\cdot}OH$ by sodium amalgam, zinc-dust and hydrochloric acid, or some other suitable reducing agent.

5. When heated with concentrated hydriodic acid and amorphous phosphorus at a high temperature, it would be converted into a hydrocarbon of the paraffin series having the constitution

$$CH_3{\cdot}[CH_2]_7{\cdot}CH_3.$$

The behaviour of the reduction product with each of the reagents just enumerated was carefully examined, in most cases the experiments being repeated several times under varied conditions; the results were, however, completely at variance with those which, in all probability, would have been obtained had the reduction product been a ketone alcohol; its constitution cannot, therefore, be represented by formula I.

On the other hand, the chemical behaviour of the reduction product is exactly what might be expected, assuming that it is a dihydroxy-compound of the constitution expressed by formula II; this will be evident from a consideration of the following facts:—

1. It does not combine with hydroxylamine or with phenylhydrazine.

2. It yields a diacetyl-derivative of the composition $C_{13}H_{22}O_4$ with acetic anhydride.

3. Phosphorus pentabromide converts it into a dibromide of the composition $C_9H_{16}Br_2$; this substance seems also to be formed with difficulty on prolonged heating with concentrated hydrobromic acid.

4. It is not acted on by such reducing agents as zinc and hydrochloric acid in alcoholic solution, sodium amalgam, sodium and alcohol.

5. On reduction with hydriodic acid and amorphous phosphorus, it is converted into a hydrocarbon of the composition C_9H_{18}.

These facts are, we believe, amply sufficient to warrant the conclusion that the reduction product of $\alpha\alpha'$-diacetylpentane is a dimethyldihydroxyheptamethylene of the constitution

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMe\cdot OH\\ CH_2\cdot CH_2\cdot CMe\cdot OH\end{matrix}.$$

The derivatives of this compound, which are referred to above, and described in the experimental part of the paper, have, therefore, the constitutions represented by the following formulæ:—

Dimethyldihydroxyheptamethylene diacetate,

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMe\cdot OAc\\ CH_2\cdot CH_2\cdot CMe\cdot OAc\end{matrix}.$$

Dimethyldibromoheptamethylene,

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMeBr\\ CH_2\cdot CH_2\cdot CMeBr\end{matrix}.$$

Dimethylheptamethylene,

$$CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CHMe\\ CH_2\cdot CH_2\cdot CHMe\end{matrix}.$$

The compounds obtained in the course of this investigation are, we believe, the first and only derivatives of the 7-carbon ring—heptamethylene—which have yet been prepared, and the constitution of which has been proved with any degree of certainty.

Markownikoff has, however, lately published an interesting paper on some compounds obtained from suberone (*Compt. rend.*, **110**, 466—468), which, including suberone itself, he considers to be derivatives of heptamethylene; and by reducing suberonyl alcohol with hydriodic acid, he obtained a hydrocarbon of the composition C_7H_{14}, which he supposes to be heptamethylene.

It appears to us that the results obtained by Markownikoff can be equally well explained on the assumption that suberone is a methylketohexamethylene, a dimethylketopentamethylene, or some other ketopolymethylene derivative, and that as yet no evidence has been brought forward to warrant the conclusion that suberone is a heptamethylene derivative.

Dimethyldihydroxyheptamethylene $CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMe\cdot OH\\ CH_2\cdot CH_2\cdot CMe\cdot OH\end{matrix}$.

Dimethyldihydroxyheptamethylene (dimethylheptamethylene glycol) and small quantities of a condensation product of high molecular weight are obtained by the reduction of $\alpha\alpha'$-diacetylpentane in the following manner:—A solution of the pure diketone in 5 to 6 times its volume of pure ether is poured into a large bottle which contains

about 150 c.c. of concentrated soda, and is provided with a reflux condenser. Sodium is then added in small portions at a time, any considerable rise of temperature being avoided by immersing the bottle in cold water. When the reduction has proceeded for some time, the metal becomes covered with a thick layer of a colourless sodium derivative of the glycol, and in some cases a considerable quantity of this compound is deposited on the sides of the vessel, but on agitating the alkaline liquid, it gradually passes into solution. The addition of sodium is continued until 6 to 8 times the quantity theoretically necessary for complete reduction, that is, 4 atoms of sodium to 1 mol. of the diketone, has been employed.

The ethereal solution is then separated, the alkaline liquid extracted once or twice with ether, the combined ethereal solutions very carefully dried over anhydrous potassium carbonate, filtered, and evaporated, when there remains a yellowish oil, the weight of which is about the same as that of the diketone employed. The crude product is submitted to fractional distillation under reduced pressure, say, 180 mm.; the thermometer quickly rises to 195°; almost the whole of the product passing over between 195° and 205°, the temperature then rises rapidly to about 300°, when a thick, yellowish oil collects in the receiver. The quantity of this compound of high boiling point is only about 3—6 per cent. of the crude reduction product; it will be referred to again hereafter.

The portion passing over between 195° and 205° consists of slightly impure dimethyldihydroxyheptamethylene, from which the pure compound can be easily obtained by submitting it to repeated fractional distillation under reduced pressure.

Analyses of various preparations of the pure compound gave the following results:—

I. 0·2016 gram substance gave 0·5062 gram CO_2 and 0·2098 gram H_2O.

II. 0·1852 gram substance gave 0·4624 gram CO_2 and 0·1923 gram H_2O.

III. 0·2112 gram substance gave 0·5266 gram CO_2 and 0·2178 gram H_2O.

	Calculated for $C_9H_{18}O_2$.	Found. I.	II.	III.
C	68·36 p. c.	68·5	68·1	68·0 p. c.
H	11·39 „	11·6	11·5	11·5 „
O	20·25 „	20·9	20·4	20·5 „

Dimethyldihydroxyheptamethylene is a moderately thick, colourless oil, with a sharp, burning taste, and a characteristic smell re-

calling that of thyme; it is specifically lighter than water, and is volatile with steam and alcohol vapour. It boils at 201° under a pressure of 180 mm., at 203—205° under a pressure of 186 mm., and at 180—185° under a pressure of 100 mm., the thermometer being entirely in the vapour in all three cases; when cooled below 0°, it becomes very thick, but shows no signs of crystallising even when kept below 0° for some time.

It is miscible with alcohol, ether, chloroform, glacial acetic acid, &c., in all proportions, but is only sparingly soluble in cold water, from which it separates again on warming or on adding sodium carbonate; it is insoluble in soda. It dissolves in concentrated sulphuric acid with development of heat, and it is also soluble in concentrated hydrobromic acid, although it quickly separates from the solution again, having been partially converted into an insoluble bromide. It does not combine with sodium hydrogen sulphite, hydroxylamine, or phenylhydrazine, but it is readily acted on by boiling acetic anhydride, yielding a diacetyl-derivative, and by phosphorus pentabromide, which converts it into an oily dibromide.

It is a curious fact that a mixture composed of about 94 per cent. of dimethyldihydroxyheptamethylene, and about 6 per cent. of water, has approximately the same boiling point as the anhydrous glycol, and is not separated into its constituents on fractional distillation under reduced pressure. This fact was brought under our notice at an early stage of the investigation in the following manner:—The ethereal solution of the crude reduction product of diacetylpentane, having been treated for a short time with anhydrous calcium chloride, was evaporated, the residue submitted to fractional distillation under a pressure of 150 mm., and the portion passing over between 197—199° collected separately.

Two analyses of this liquid gave the following results:—

I. 0·1760 gram substance gave 0·4161 gram CO_2 and 0·1854 gram H_2O.

II. 0·1432 gram substance gave 0·3386 gram CO_2 and 0·1528 gram H_2O.

	Calculated for $C_9H_{18}O_2$ + 6 p. c. H_2O.	Found. I.	Found. II.
C	64·3 per cent.	64·5	64·5 per cent.
H	11·4 „	11·7	11·7 „
O	24·3 „	23·8	23·8 „

This fraction (b. p. 197—199°; 150 mm.) was distilled again under a pressure of 100 mm., the portion passing over between 182° and 186° collected separately, and analysed:—

0·1640 gram substance gave 0·3850 gram CO_2 and 0·1737 gram H_2O.

	Calculated for $C_9H_{18}O_2$ + 6 p. c. of H_2O.	Found.
C	64·3 per cent.	64·6 per cent.
H	11·4 „	11·7 „
O	24·3 „	23·7 „

Water is, doubtless, the impurity to which the low percentage of carbon found is due, because when anhydrous potassium carbonate is employed for drying the ethereal solution, other conditions remaining the same, the glycol is easily obtained in a pure condition; the experiments show, moreover, that the water cannot be eliminated by fractional distillation, just as is the case with other mixtures of like nature.

Sodium Derivative of Dimethyldihydroxyheptamethylene.

This compound frequently separates from the ethereal solution in the preparation of dimethyldihydroxyheptamethylene in the manner described above. In order to determine its composition, some of the substance adhering to the sides of the bottle, and out of contact with the aqueous alkali, was picked out, quickly washed with ether on a porous plate, and then kept for some days in a desiccator.

The analyses of three different samples obtained in this way, and quickly weighed from stoppered bottles, gave the following results:—

I. 0·3362 gram substance gave 0·1156 gram Na_2SO_4.
II. 0·2932 „ „ 0·1022 „
III. 0·3254 „ „ 0 1112 „

	Calculated for $C_9H_{17}O_2Na$ + H_2O.	Found. I.	II.	III.
Na.....	11·5 per cent.	11·1	11·3	11·1 per cent.

These analyses show that the compound is a mono-sodium derivative of the glycol, containing, very probably, 1 mol. of water. In spite of the hygroscopic nature of the substance, there is no reason to suppose that this view of its composition is incorrect, since ethyl sodacetoacetate and other compounds of like nature have been proved to contain water of crystallisation.

The sodium derivative of the glycol is a colourless, semi-crystalline, deliquescent compound which gradually decomposes on exposure to the air or when heated at about 50—60° in the air; it melts below 100°, and is quickly decomposed by cold water, but rather slowly by very concentrated soda.

It is, perhaps, unnecessary to remark that the formation of a mono- instead of a di-sodium derivative, under the conditions described above, cannot be regarded as evidence against the view that the reduction product is a dihydroxyheptamethylene derivative.

Constitution of Dimethyldihydroxyheptamethylene.

In accordance with the views put forward in the introduction, the reduction product of diacetylpentane may, theoretically, have the constitution represented by one of two formulæ (p. 215); in one case it would be an open-chain ketone-alcohol, in the other a closed-chain dihydric alcohol. It was necessary, therefore, in the first place, to investigate its behaviour with phenylhydrazine and with hydroxylamine; the following experiments were made for this purpose.

Behaviour of the Reduction Product with Phenylhydrazine.—A small quantity (3 grams) of the crude reduction product was heated at about 100° for three hours in sealed tubes with phenylhydrazine hydrochloride (4·8 grams) and sodium acetate (4·5 grams) in dilute alcoholic solution. The clear solution was then diluted with a large volume of water, the precipitated oil extracted with ether, the ethereal extract washed with very dilute hydrochloric acid, dried over calcium chloride, and evaporated. The yellowish, oily product weighed 2·8 grams, and showed all the properties of the original reduction product; a qualitative examination showed that it contained a trace of nitrogen, but the quantity was so small that it was quite evident that the formation of a hydrazone had not taken place.

Behaviour of the Reduction Product with Hydroxylamine.—Two experiments were made under different conditions, in order to try and prepare an oxime of the reduction product of diacetylpentane, but both were unsuccessful. In the first, the crude reduction product (4 grams) was treated with hydroxylamine hydrochloride (4 grams) and potassium carbonate (3 grams) in dilute alcoholic solution for three days at the ordinary temperature. After evaporating most of the alcohol on the water-bath, the residue was extracted with ether, the solution dried over calcium chloride, and evaporated, when there remained a light-yellow oil (3·8 grams); this oil contained a trace of nitrogen, but was insoluble in alkalis, and possessed all the properties of the original reduction product.

In the second experiment, the pure compound (3 grams) was treated with hydroxylamine hydrochloride (1·4 grams) and potash (5 grams) in dilute methyl alcoholic solution according to Auwers' method. After keeping the mixture for two days at the ordinary temperature, the alcohol was evaporated, the oil extracted with ether, the ethereal solution washed with very dilute hydrochloric acid, dried

over calcium chloride, and evaporated. There remained a yellowish oil (2·4 grams) which did not contain a trace of nitrogen, and which showed all the properties of the original compound.

Behaviour of the Reduction Product with Reducing Agents.—Although the above experiments had shown pretty conclusively that the reduction product does not contain a carbonyl group, it seemed advisable to obtain further experimental proof that such is in reality the case by investigating its behaviour with reducing agents in the manner described below:—

Exp. 1.—The pure reduction product (about 20 grams) was dissolved in alcohol, and zinc-dust and hydrochloric acid added to the boiling solution in small portions at a time, the operation taking about three hours; the solution was then diluted with water, the precipitated oil extracted with ether, and again submitted to the same treatment with zinc-dust and hydrochloric acid. Finally, the product was fractionated, and the portion passing over between 205° and 215° (210 mm.), which formed about 70 per cent. of the whole, collected separately and analysed; the percentage of hydrogen was found to be 11·6, proving that in this case also reduction had not taken place.

Exp. 2.—The original reduction product was dissolved in dilute alcohol, and a large quantity of sodium amalgam added to the boiling solution, in small portions at a time. The product, isolated in the usual manner, was fractionated under a pressure of about 280 mm., and the portion boiling at 200—210° collected for analysis. It was found to contain 11·57 per cent. of hydrogen, and to possess all the properties of the original compound.

Exp. 3.—The pure compound (16 grams) was dissolved in alcohol (100 grams), and sodium added in small portions at a time, the process being continued until a large excess (26 grams) of the metal had been employed, dilute alcohol being added from time to time whenever the reaction began to slacken. The alcohol was then evaporated as completely as possible, the residue diluted with water, the precipitated oil extracted with ether, dried, and fractionated under reduced pressure. Two analyses, made with different portions of the product, gave 11·72 and 11·76 per cent. of hydrogen respectively, proving conclusively that reduction had not taken place, since the addition of 2 atoms of hydrogen to the original reduction product would increase the percentage of hydrogen from 11·4 to 12·5 per cent.

Up to this stage of the investigation, it had been proved that the reduction product of diacetylpentane cannot be a ketone-alcohol of the constitution represented by formula I (p. 215); the following experiments show that it is a dihydric alcohol of the composition $C_9H_{18}O_2$.

Dimethyldibromoheptamethylene, $CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMeBr\\ CH_2\cdot CH_2\cdot CMeBr\end{matrix}$.

When the reduction product is treated with phosphorus pentabromide under suitable conditions, it is converted into a dibromide of the composition $C_9H_{16}Br_2$, which has, doubtless, the constitution assigned to it above. Before describing the preparation and properties of this dibromide, it will be as well, perhaps, to give a short account of the behaviour of the reduction product with hydrobromic acid.

A considerable quantity of the pure compound was heated at 100—115° in sealed tubes for about two hours with five times its volume of concentrated hydrobromic acid; on opening the tubes, it was found that the contents had separated into two layers, the upper one consisting of a dark-coloured oil. This oil was extracted from the diluted and partially neutralised solution by means of ether, the ethereal extract washed, dried, and evaporated, and the residue distilled under reduced pressure (about 140 mm.). The whole passed over between 160° and 220°, but no constant boiling point could be observed; the portion boiling at 160—200° was collected and analysed, and found to contain only 39 per cent. of bromine. As a compound of the composition $C_9H_{17}BrO$ contains 36·1, and a compound of the composition $C_9H_{16}Br_2$ 56·3 per cent. of bromine, it would seem that the liquid analysed consisted principally of the monobromide. In order to try and convert it into the dibromide, the whole of the distilled product was again heated at about 120° for several hours with a large excess of concentrated hydrobromic acid. The dark reddish-brown, heavy oil, obtained in this way, was distilled under a pressure of about 70 mm., and the portion boiling at 160—167° collected separately; the analysis of this fraction gave the following result:—

0·1758 gram substance gave 0·2047 gram AgBr.

	Calculated for		
	$C_9H_{17}BrO$.	$C_9H_{16}Br_2$.	Found.
Br.....	36·1 p. c.	56·3 p. c.	49·5 p. c.

These experiments show that the reduction product is partially converted into a dibromide by concentrated hydrobromic acid, a fact which is of considerable importance as a proof that it is a dihydric alcohol; as, however, the change is only incomplete even after prolonged heating with the acid, a more suitable method had to be employed for the preparation of the dibromide.

For this purpose, a small quantity of the pure reduction product

is dissolved in a large volume of anhydrous chloroform, and a fair excess of the theoretical quantity of phosphorus pentabromide gradually added; evolution of hydrogen bromide quickly commences, and, after keeping for some time at the ordinary temperature, the reaction is at an end. The solution is decanted from the unchanged pentabromide, poured into cold water, and as soon as the decomposition of the phosphorus oxybromide is complete, the chloroform solution of the dibromide is separated, washed with dilute sodium carbonate and water consecutively, dried over calcium chloride, and the chloroform evaporated on the water-bath, when dimethyldibromoheptamethylene remains as a thick yellowish oil.

A bromine determination, made with a portion of the product which had been kept for 24 hours over sulphuric acid and paraffin, gave the following result:—

0·1036 gram substance gave 0·1370 gram AgBr.

	Calculated for $C_9H_{16}Br_2$.	Found.
Br	56·3 per cent.	54·8 per cent.

Dimethyldibromoheptamethylene is a thick, almost colourless oil with a sweetish, rather unpleasant smell; it is specifically heavier than, and insoluble in, water, but miscible with most ordinary organic solvents in all proportions. It seems to undergo slight decomposition when it is kept over sulphuric acid under reduced pressure.

Dimethylhydroxyiodoheptamethylene, $CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMeI\\ CH_2\cdot CH_2\cdot CMe\cdot OH\end{matrix}$.

When the glycol obtained from diacetylpentane is heated with hydriodic acid of sp. gr. 1·96, it seems to be almost completely converted into the moniodide, $C_9H_{17}OI$; the diiodide, $C_9H_{16}I_2$, if produced at all, is only formed in very small quantities.

The moniodide was prepared in the following manner:—The pure glycol was mixed with a considerable quantity of hydriodic acid of sp. gr. 1·96, and the mixture heated on the water-bath in a flask provided with a reflux condenser, first at a moderately low temperature, and then for about two hours at 100°. A portion of the contents of the flask was then distilled off, because it was thought that the diiodide would probably be more volatile than the moniodide, and if any of the former had been produced, it would collect in the receiver, leaving the moniodide behind. The small quantity of oil in the acid distillate was extracted with ether, the solution washed with dilute sodium carbonate and water, consecutively, dried over calcium

chloride, and evaporated. The colourless oil obtained in this way was kept over sulphuric acid under reduced pressure for about 12 hours, and then an iodine determination carried out with the following result:—

0·1735 gram substance gave 0·1622 gram AgI.

	Calculated for $C_9H_{17}IO$.	Found.
I	47·29 per cent.	50·49 per cent.

The compound obtained by distillation as described above evidently consists principally of the moniodide, but contains a little of the diiodide; the former can be isolated in a pure condition from the residue in the flask by extracting with ether, and evaporating the washed and dried solution.

A portion of the oil (which remained in the flask) was kept under reduced pressure, and analysed with the following result:—

0·1661 gram substance gave 0·1455 gram AgI.

	Calculated for $C_9H_{17}IO$.	Found.
I	47·29 per cent.	47 06 per cent.

Dimethylhydroxyiodoheptamethylene is a colourless, mobile oil with a pleasant sweetish smell; it is readily soluble in ether, alcohol, and most ordinary organic solvents, but insoluble in water. It gradually decomposes, and turns brown on keeping, but it seems to boil without decomposition when heated in small quantities under the ordinary pressure.

Dimethylheptamethylene Diacetate, $CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CMe\cdot OAc\\ CH_2\cdot CH_2\cdot CMe\cdot OAc\end{matrix}$.

When the reduction product of diacetylpentane is treated with acetic anhydride under suitable conditions, it is completely converted into a diacetyl derivative of the composition $C_9H_{16}(OAc)_2$; the formation of this diacetyl derivative is one of the strongest proofs that the compound described above as dimethyldihydroxyheptamethylene contains two hydroxy-groups.

In preparing the diacetyl derivative, the pure glycol is dissolved in excess of acetic anhydride, and the mixture boiled for about $2\frac{1}{2}$ hours in a flask provided with a reflux condenser; the acetic anhydride is then partially distilled off under the ordinary pressure, and the residue submitted to fractional distillation under a pressure of 65 mm. The thermometer rises rapidly to about 180°, a small quantity only passing over below 190°; the thermometer then remains

fairly constant, and between 192° and 207° about 70 per cent. of the whole passes over, the thermometer finally rising to about 215°.

The fraction boiling at 192—207° was fractionated again under the same pressure, and the portion boiling constantly at 199—202° collected separately.

The analysis of this fraction gave results which agreed well with those required by a diacetyl derivative of dimethyldihydroxyheptamethylene.

0·1555 gram substance gave 0·3681 gram CO_2 and 0·1323 gram H_2O.

	Calculated for $C_9H_{16}(OAc)_2$.	Found.
C.....	64·5 per cent.	64·67 per cent.
H.....	9·1 ,,	9·45 ,,
O.....	26·4 ,,	25·88 ,,

As, however, a monacetyl-derivative of the composition $COMe\cdot[CH_2]_5\cdot CHMe\cdot OAc$ would have approximately the same composition (C = 66·0 per cent., H = 10·0 per cent., O = 24 per cent.), elementary analysis alone is not sufficient to prove beyond doubt that the compound is really a diacetyl derivative. As this point was of the utmost importance in deciding between the two possible formulæ for the reduction product, the quantity of acetic acid given on hydrolysis was determined. Three estimations of this kind were made; in each case, a weighed quantity of the pure compound was boiled with excess of standard potash, and the excess of alkali determined by titration with standard sulphuric acid, phenolphthaleïn being used as indicator.

The following results were obtained:—

I. 1·169 gram substance was boiled for $1\frac{1}{2}$ hours with 150 c.c. of potash (1 c.c. = 0·00597 gram of $C_2H_4O_2$), and the cold solution titrated with sulphuric acid of the same strength; 56·4 c.c. of acid were required, showing that 93·6 c.c. of potash had been neutralised.

II. 0·8638 gram substance was boiled for two hours with 100 c.c. of potash, and the solution titrated with sulphuric acid; 44·3 c.c. of acid were required.

III. 0·5676 gram substance was boiled for an hour with 100 c.c. of potash, and the cold solution titrated; 54·7 c.c. of sulphuric acid were required.

	Calculated for $C_9H_{16}(OAc)_2$.	Found.		
		I.	II.	III.
$C_2H_4O_2$.....	49·58 p. c.	47·8	48·4	47·6 p. c.

These results show conclusively that the compound in question is a diacetyl derivative, and, consequently, the presence of two hydroxy-groups in the original reduction product may be considered as proved.

Dimethylheptamethylene diacetate is a colourless, mobile liquid possessing a sweet, rather pleasant smell, and boiling at 199—202° under a pressure of 65 mm. It seems to be insoluble in cold water, but is readily soluble in alcohol, ether, acetic anhydride, and other organic solvents. It is readily hydrolysed even by very dilute aqueous potash, as is shown by the quantitative experiments referred to above.

Dimethylheptamethylene, $CH_2<\begin{matrix}CH_2\cdot CH_2\cdot CHMe\\ CH_2\cdot CH_2\cdot CHMe\end{matrix}$.

One of the most important facts that can be adduced in favour of the closed-chain formula for the reduction product of diacetylpentane is that, when treated with hydriodic acid and amorphous phosphorus at a high temperature, it is converted into a hydrocarbon of the molecular formula C_9H_{18}, which, from its method of formation must be a saturated compound. This hydrocarbon, dimethylheptamethylene, is obtained in the following way:—The pure glycol is first heated for about two hours at 100° in a flask provided with a reflux condenser, with excess of concentrated hydriodic acid, in order to convert it into the moniodide described above; this product is isolated in the usual manner, and then heated in sealed tubes at 230—260° for 8 to 10 hours with a large excess of hydriodic acid of sp. gr. 1·96, and a little amorphous phosphorus, about 4 grams only of the crude iodide being placed in each tube. When the tubes were opened, the hydrocarbon, which formed a lighter-coloured layer on the surface of the acid, was separated with the aid of a funnel, washed well with sodium carbonate, dried over potassium carbonate, and distilled. The thermometer rose at once to about 145°, and between 145° and 160° almost three-quarters of the crude product passed over; the liquid which then remained in the flask boiled at a very much higher temperature, and was not examined further, owing to its small quantity. The fraction boiling at 145—160° was then distilled two or three times over potassium, and finally a sample of the liquid boiling constantly at 153—154° was collected separately for analysis.

The results obtained were the following:—

0·1300 gram substance gave 0·4072 gram CO_2 and 0·1717 gram H_2O.

	Calculated for C_9H_{18}.	Found.
C	85·7 per cent.	85·42 per cent.
H	14·3 ,,	14·67 ,,

A vapour density determination carried out in Hofmann's apparatus, and employing aniline as the heating vapour, gave the following result:—

0·0782 gram substance gave 68 c.c. of vapour. Barometer = 748 mm. Difference of level 490 mm. Temperature of vapour 184°, and of air 11°.

	Calculated for C_9H_{18}.	Found.
V.D.	63	61·2

Two elementary analyses of a sample of the hydrocarbon from another preparation gave the following results:—

I. 0·1271 gram substance gave 0·3965 gram CO_2 and 0·1702 gram H_2O.

II. 0·1192 gram substance gave 0·3727 gram CO_2 and 0·1588 gram H_2O.

	Calculated for C_9H_{18}.	Found. I.	Found. II.
C	85·7 p. c.	85·08	85·14 p. c.
H	14·3 „	14·88	14·83 „

Dimethylheptamethylene is a colourless mobile, strongly refractive liquid with an odour very like that of light petroleum; it boils at 153° under the ordinary atmospheric pressure. It is insoluble in water, and in concentrated hydriodic acid, but is miscible with organic solvents in all proportions. It seems to be a very stable substance, but owing to the small quantity at our disposal, we have not been able to investigate its properties as completely as would be desirable. It is not acted on by concentrated hydriodic acid; when treated with concentrated nitric acid, a reaction soon sets in, heat is developed, and dense brown fumes are evolved, but the reaction soon slackens, and heat must be applied before complete solution ensues; as far as our experiments went, no compounds other than acids of low molecular weight are formed by the oxidation of the hydrocarbon in this way.

Condensation Product of Dimethyldihydroxyheptamethylene.

It has been mentioned above that in the preparation of dimethyldihydroxyheptamethylene there is formed in small quantities a liquid of considerably higher boiling point, which seemed to be a condensation product of the glycol. In order to investigate the nature of this compound, the residues obtained in several operations were united, and the liquid submitted to fractional distillation under a

pressure of about 200 mm.; at first, a small quantity of dimethyldihydroxyheptamethylene passed over, and then the thermometer rose rapidly to about 300°, the remainder boiling almost constantly at 305—310°.

This high boiling liquid gave the following result on analysis:—

0·2011 gram substance gave 0·4143 gram CO_2, and 0·2082 gram H_2O.

	Calculated for $C_{18}H_{34}O_3$.	Found.
C.....	72·48 per cent.	72·6 per cent.
H.....	11·41 „	11·4 „
O.....	16·11 „	16·0 „

A molecular weight determination by Raoult's method in glacial acetic acid solution gave the following data:—

0·9116 gram substance dissolved in 43·1 grams acetic acid lowered the melting point 0·271, as a mean of two closely agreeing observations.

	Calculated for $C_{18}H_{34}O_3$.	Found.
M. W.....	298	305

This result shows that the compound in question has been formed by the condensation of two molecules of diacetylpentane, or its reduction product; the analysis given above agrees very well with the formula $C_{18}H_{34}O_3$, but not so well with the formula $C_{18}H_{32}O_3$, which would require 72·9 per cent. of carbon and 10·8 per cent. of hydrogen. Considering, also, that a large excess of sodium was invariably employed in the reduction of diacetylpentane, and that the only other product is the glycol $C_9H_{18}O_2$, it seems almost certain that the condensation product is formed from the glycol, and not from the ketone, according to the equation

$$2C_9H_{18}O_2 = C_{18}H_{34}O_3 + H_2O.$$

just as diethylene glycol is formed from two molecules of ethylene glycol with elimination of one molecule of water.

The condensation product of the heptamethylene derivative has no well-defined properties; it is an almost colourless, very thick oil, boils at about 305—310° (200 mm. pressure), and shows no signs of crystallising even when kept for months at the ordinary temperature, or for some hours in a freezing mixture. It is insoluble in water, but the ordinary organic solvents dissolve it in large quantities.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, April*, 1890. Vol. LVII.]

DERIVATIVES OF PHENYLHEXAMETHYLENE.*

By F. Stanley Kipping, Ph.D., D.Sc., and W. H. Perkin, Jun., Ph.D.

In a paper published some time since (Trans., 1887, 51, 717), it was shown that methyldehydrohexonecarboxylic acid, when boiled with water, is converted into acetobutyl alcohol and carbonic anhydride, thus :—

$$\begin{matrix} CH_3\cdot C\!-\!O\!-\!CH_2 \\ COOH\cdot C\cdot CH_2\cdot CH_2 \end{matrix} + H_2O = CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH + CO_2.$$

In studying the action of water on phenyldehydrohexonecarboxylic acid (*loc. cit.*, p. 733), a similar change was found to take place, the acid decomposing into benzoylbutyl alcohol,

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH,$$

and carbonic anhydride.

* *Cf.*, *Chem. Soc. Proceedings*, 1889, 161.

The two analogously constituted alcohols thus obtained exhibit a most remarkable difference in point of stability. Acetobutyl alcohol boils with only very slight decomposition at 226—227°, whereas benzoylbutyl alcohol, when only gently warmed, is decomposed at once into phenyldehydrohexone and water, thus:—

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH = C_6H_5\cdot \begin{matrix} C & -O- & CH_2 \\ \| & & | \\ CH & \cdot CH_2 & CH_2 \end{matrix} + H_2O.$$

The tendency of this alcohol to undergo internal condensation is so great, that when the crystalline substance is placed over sulphuric acid, the crystals are soon converted into a colourless oil, which on investigation was found to consist of pure phenyldehydrohexone. This remarkable behaviour, and the fact that benzoylbutyl alcohol had only been obtained in very small quantities, and therefore very imperfectly examined, made it advisable to repeat the experiments with larger quantities, in order to study the points of resemblance and difference between this alcohol and acetobutyl alcohol.

A considerable quantity of phenyl dehydrohexonecarboxylic acid was therefore prepared, dissolved in ammonia, reprecipitated by a dilute acid, and the resulting finely-divided substance boiled with a large quantity of water for some hours on a reflux apparatus. As soon as the evolution of carbonic anhydride had ceased, the flask was put on one side, and allowed to cool slowly.

The solution, which soon becomes turbid, deposits a considerable quantity of the benzoylbutyl alcohol in oily drops, which solidify on cooling; but in some cases the liquid becomes filled with large, transparent, leafy crystals. These beautiful crystals melt at 40—41°, and do not change when kept for months under ordinary conditions; but if a crystal is placed over sulphuric acid in a desiccator, in the course of half-an-hour, and often in a very few minutes, it entirely disappears, leaving an oily residue of pure phenyldehydrohexone. The same change naturally takes place when the crystals are heated, but boiling with water seems to have little effect on them.

Benzoylbutyl alcohol and hydroxylamine combine readily, yielding a crystalline oxime, $C_6H_5\cdot C(NOH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$, melting at 56—57°.

Sodium amalgam converts it into phenylpentamethylene glycol:—

$$C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH + H_2 = C_6H_5\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH.$$

This glycol crystallises in needles which melt at about 54°; it is far more stable than benzoylbutyl alcohol, and may be kept over sulphuric acid under reduced pressure for apparently any length of time without change.

This behaviour is in accordance with previous observations, as it has been found that the ketone alcohols are invariably less stable than the glycols obtained from them by reduction.

The preparation of phenylpentamethylene dibromide,

$$C_6H_5\cdot CHBr\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br,$$

from the glycol was found to be a rather difficult matter, because when the glycol is treated with a fuming solution of hydrogen bromide, the monobromide which is first formed is so insoluble that very little further action takes place, except at temperatures so high that the resulting dibromide suffers decomposition.

Pure phenylpentamethylene dibromide was, however, ultimately prepared by the action of phosphorus pentabromide on the chloroform solution of the glycol. It is a thick, almost colourless oil, which on standing becomes slightly yellowish.

In a previous communication, by P. C. Freer and one of us (Trans., 1888, **53**, 202), it was shown that when ethyl sodiomalonate or ethyl sodioacetoacetate is treated with methylpentamethylene dibromide, derivatives of methylhexamethylene, $\begin{matrix}CH_3\cdot CH\cdot CH_2\cdot CH_2\\ \quad\quad\quad\quad\quad\quad |\\ CH_2\cdot CH_2\cdot CH_2\end{matrix}$, are formed. It appeared very interesting to determine whether analogous derivatives of phenylhexamethylene (hexahydrodiphenyl), $CH\begin{matrix}<CH\cdot CH\\ <CH{:}CH\end{matrix}>C\cdot CH<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH_2$, could be obtained in like manner from phenylpentamethylene bromide. The experiments instituted with this object are, briefly described, the following:—

Ethyl malonate (2 mols.), sodium ethoxide (2 mols.), and phenylpentamethylene dibromide (1 mol.) were digested together in alcoholic solution for some time. An action sets in readily, and a thick, yellow oil is formed, which, as shown by its behaviour on hydrolysis, undoubtedly contains ethyl phenylhexamethylenedicarboxylate (2 : 1 : 1).

$$2CHNa(COOC_2H_5)_2 + C_6H_5\cdot CHBr\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br = \begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\quad\quad\quad\quad |\\ CH_2\cdot CH_2\cdot C(COOC_2H_5)_2\end{matrix} + CH_2(COOC_2H_5)_2 + 2NaBr.$$

Ethyl phenylhexamethylenedicarboxylate.

On hydrolysis, this ethereal salt yields the dicarboxylic acid, which, when heated at 160°, is resolved into carbonic anhydride and phenylhexamethylenecarboxylic acid (2 : 1).

$$\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\quad\quad\quad\quad |\\ CH_2\cdot CH_2\cdot C(COOH)_2\end{matrix} = \begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\quad\quad\quad\quad |\\ CH_2\cdot CH_2\cdot CH\cdot COOH\end{matrix} + CO_2.$$

Phenylhexamethylenedicarboxylic acid (2 : 1 : 1). Phenylhexamethylenemonocarboxylic acid (2 : 1).

During this operation the liquid gets darker and darker, owing to partial decomposition, and the resulting dark-brown oily acid is extremely difficult to purify; it was, however, obtained in a pure condition by conversion, first into the barium salt, and then into the crystalline ammonium salt, which was subsequently decomposed with dilute sulphuric acid.

Phenylhexamethylenemonocarboxylic acid crystallises from light petroleum in compact, well-defined prisms which melt at 104—105°. Its solution in carbonate of soda does not decolorise potassium permanganate, even when allowed to stand for some time. This behaviour shows that this acid is a saturated compound (compare von Baeyer, *Annalen*, **245**, 147), and it must therefore have the constitution assigned to it above.

In studying the action of methylpentamethylene dibromide on ethyl sodiomalonate and ethyl sodioacetoacetate, it was found that hexamethylene-derivatives are formed in both cases (Freer and Perkin, Trans., 1888, **53**, 204. Compare "Action of Trimethylene Bromide on Ethyl Sodioacetoacetate," Trans., 1887, **51**, 709).

It appeared probable, therefore, that if ethyl acetoacetate was substituted for ethyl malonate, the crude product would, on hydrolysis, yield phenylhexamethylenecarboxylic acid. Our experiments in this direction have fully borne out these expectations.

Phenylpentamethylene dibromide and ethyl sodioacetoacetate react readily, when warmed together in alcoholic solution, with formation of a yellowish oil, which, as is seen from its decomposition on hydrolysis, is evidently ethyl acetylphenylhexamethylenecarboxylate (1 : 2 : 1).

$$\text{I.}\quad \begin{matrix}CH_3\cdot CO\\ COOC_2H_5\end{matrix}\!>\!CHNa + C_6H_5\cdot CHBr\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br =$$

$$\begin{matrix}CH_3\cdot CO\\ COOC_2H_5\end{matrix}\!>\!CH\cdot CH(C_6H_5)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br + NaBr.$$

$$\text{II.}\quad \begin{matrix}CH_3\cdot CO\\ COOC_2H_5\end{matrix}\!>\!CH\cdot CH(C_6H_5)\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2Br + C_2H_5\cdot ONa$$

$$= \begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\qquad\qquad |\\ CH_2\cdot CH_2\cdot C(CO\cdot CH_3)\cdot COOC_2H_5\end{matrix} + NaBr + C_2H_5\cdot OH.$$

Ethylic acetylphenylhexamethylene-carboxylate (1 : 2 : 1).

On hydrolysis, the crude ethereal salt yields phenylhexamethylene-carboxylic acid and phenylhexamethylene methyl ketone, thus:—

I. $\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\\ CH_2\cdot CH_2\cdot C(CO\cdot CH_3)\cdot COOC_2H_5\end{matrix}$ + 2KOH =

$\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\\ CH_2\cdot CH_2\cdot CH\cdot COOK\end{matrix}$ + $CH_3\cdot COOK$ + $C_2H_5\cdot OH$.

Potassium phenylhexamethylene-carboxylate (2 : 1).

II. $\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\\ CH_2\cdot CH_2\cdot C(CO\cdot CH_3)\cdot COOC_2H_5\end{matrix}$ + 2KOH =

$\begin{matrix}CH_2\cdot CH_2\cdot CH\cdot C_6H_5\\ |\\ CH_2\cdot CH_2\cdot CH\cdot CO\cdot CH_3\end{matrix}$ + $C_2H_5\cdot OH$ + K_2CO_3.

Phenylhexamethylene methyl ketone (2 : 1).

The phenylhexamethylenecarboxylic acid obtained by this method is rather easier to purify than that formed by the decomposition of the dicarboxylic acid. A careful comparison of the two products has shown that they are identical.

Phenylhexamethylene methyl ketone is produced in small quantity by the hydrolysis of ethylic acetylphenylhexamethylenecarboxylate with potassium hydrate; it crystallises in needles which melt at about 78—79°. It combines readily with hydroxylamine forming a syrupy hydroxime, which was not obtained in a crystalline condition.

Phenyldehydrohexonecarboxylic Acid.

In preparing phenyldehydrohexonecarboxylic acid the following method has been found to give the best results:—

Ethyl benzoylacetate (50 grams) is gradually added in small portions at a time to a solution of sodium (6 grams) in absolute alcohol (72 grams), the mixture being well cooled after each addition of the ethereal salt; the trimethylene bromide (52·5 grams) is then added, and the solution heated on the water-bath for about an hour in a flask provided with a reflux condenser. The flask is then cooled under the tap, an alcoholic solution of sodium (6 grams) added in small quantities at a time to the well-cooled solution, and the mixture heated again on the water-bath for about two hours. After distilling off the alcohol, the residue is treated with water, the oil extracted with ether, and the ethereal solution dried and evaporated.

Ethyl phenyldehydrohexonecarboxylate (58 grams) is thus obtained as a thick, brown oil, which, on cooling, partially solidifies; after keeping for about 24 hours, the crystals are separated by filtration and washed with a little alcohol. The yield of the pure crystalline compound is, on the average, 17·5 grams from 50 grams of ethyl benzoylacetate; the mother liquors still contain a large quantity of

ethyl phenyldehydrohexonecarboxylate, which cannot easily be isolated, but from which it is not difficult to obtain a considerable quantity of the pure acid in the manner described below.

Phenyldehydrohexonecarboxylic acid is easily obtained in a pure condition by boiling the crystalline ethereal salt with a concentrated solution of alcoholic potash; after distilling off the alcohol, the residue is dissolved in water, the cold solution acidified with dilute sulphuric acid, the precipitated acid separated by filtration, washed with cold water, and recrystallised from alcohol. The yield is almost theoretical, 17·5 grams of the crystalline ethereal salt giving 15·3 grams of the pure acid.

A further quantity of the acid can be obtained by hydrolysing the oily mother liquors from the crystalline ethyl phenyldehydrohexonecarboxylate, as described above; after boiling for about six hours, the alcohol is distilled off, the residue treated with water, and the solution extracted twice with ether to remove acetophenone and other oily impurities. The alkaline solution is then acidified with dilute sulphuric acid, and the precipitated oil extracted with ether. On evaporating the dried ethereal solution, there remains a dark-brown oil, which soon solidifies. This product is a mixture of benzoic acid and phenyldehydrohexonecarboxylic acid; it is first spread on a porous plate to free it from small quantities of oily impurities, and then fractionally recrystallised from alcohol. In this way about 6 grams of pure phenyldehydrohexonecarboxylic acid can be obtained from the oily mother liquors produced from 50 grams of ethyl benzoylacetate, so that the total yield of the pure acid is about 23·5 grams from 50 grams of ethyl benzoylacetate.

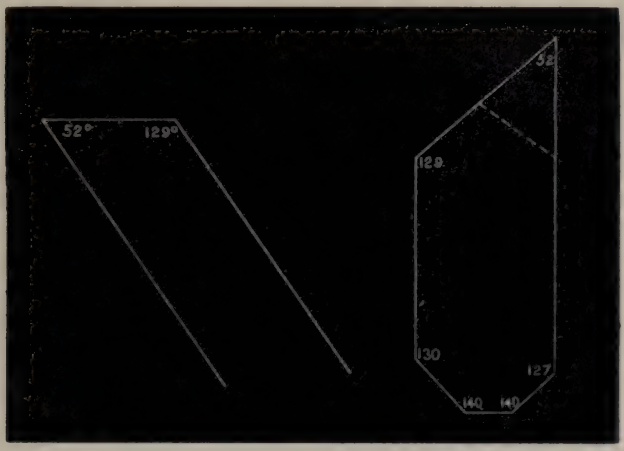
Benzoylbutyl Alcohol, $COPh\cdot[CH_2]_3\cdot CH_2\cdot OH$.

The benzoylbutyl alcohol employed in these experiments was prepared as previously described (Trans., 1887, **51**, 733), namely, by boiling finely-divided phenyldehydrohexonecarboxylic acid with a large volume of water. As soon as the evolution of carbonic anhydride is at an end, the hot solution is filtered in order to separate the phenyldehydrohexone, which is produced in considerable quantities, especially if only comparatively small quantities of water are employed. When the aqueous solution is allowed to cool slowly, some of the ketone alcohol separates in an oily condition, but when kept for a long time in the cold, the oil gradually solidifies and a considerable quantity of beautiful, iridescent crystals are obtained. As benzoylbutyl alcohol had not, up to this time, been obtained in a crystalline condition, the crystals were separated by filtration, dried for about three days on a porous plate, and then analysed with the following result--

0·2252 gram of substance gave 0·6110 gram of CO_2 and 0·1597 gram of H_2O.

	Calculated for $C_{11}H_{14}O_2$.	Found.
C	74·15 per cent.	73·99 per cent.
H	7·87 „	7·87 „
O	17·98 „	18·14 „

Benzoylbutyl alcohol crystallises from water in beautiful, iridescent, transparent plates melting at 40—41°. Some of the crystals were measured under a microscope provided with a graduated circle; the measurements are given in the following diagram.



It is readily soluble in alcohol, methyl alcohol, ether, benzene, and most of the ordinary organic solvents, but only very sparingly in light petroleum.

When the crystalline benzoylbutyl alcohol is placed in a desiccator over sulphuric acid, it rapidly liquefies and is completely converted into phenyldehydrohexone according to the equation—

$$COPh\cdot[CH_2]_3\cdot CH_2\cdot OH = CH_2<\begin{matrix}CH{:}CPh\\ CH_2\cdot CH_2\end{matrix}>O + H_2O.$$

Benzoylbutyl Alcohol Oxime, $OH\cdot N{:}CPh\cdot[CH_2]_3\cdot CH_2\cdot OH$.

Benzoylbutyl alcohol oxime is prepared by treating the crystalline ketone alcohol (1 gram) with hydroxylamine hydrochloride (0·5 gram) and potash (3 grams) in cold dilute alcoholic solution. After keeping for about 24 hours at the ordinary temperature, the alcohol is

evaporated on the water-bath, the residue treated with water, the solution slightly acidified with dilute sulphuric acid, and the precipitated oil extracted with ether. The thick, yellowish oil (1 gram) which remains when the ether is evaporated was kept over sulphuric acid under reduced pressure for about two days, and then analysed with the following result—

0·2109 gram of substance gave 12·4 c.c. of nitrogen measured at 20° and 752 mm.

	Calculated for $C_{11}H_{15}NO_2$.	Found.
N	7·25 per cent.	7·31 per cent.

After keeping the oil for some weeks in a desiccator, it showed signs of crystallising, and on rubbing it with a glass rod the whole solidified to a colourless, crystalline mass. The crystals were spread on a plate to free them from traces of oil, then dissolved in warm benzene, and the solution allowed to cool slowly.

Benzoylbutyl alcohol oxime is thus obtained in transparent microscopic plates melting at 56—57°. It is very readily soluble in chloroform, methyl alcohol, warm benzene, and most organic solvents, but only sparingly in light petroleum and in water; it dissolves freely in potash, in hydrochloric acid, and in concentrated sulphuric acid with development of heat, yielding a colourless solution. It is acted on by acetic chloride with development of heat; when the excess of acetic chloride is evaporated and the residual oil warmed, it assumes first a beautiful blue and then a red colour.

ω-Phenylpentamethylene Glycol, $OH\cdot CHPh\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$.

Phenylpentamethylene glycol is easily obtained by reducing benzoylbutyl alcohol with sodium amalgam in aqueous solution: the yield is quantitative.

In preparing the glycol it is unnecessary to isolate the benzoylbutyl alcohol; the solution of the ketone alcohol obtained by boiling phenyldehydrohexonecarboxylic acid with water is filtered from the phenyldehydrohexone, allowed to cool, placed in a large, flat-bottomed dish, and treated with a large excess of 3 per cent. sodium amalgam in small quantities at a time. If the solution is not too concentrated, it remains almost perfectly clear during the whole operation, but if a saturated solution of the ketone alcohol is employed, it soon becomes turbid, owing to the separation of oily drops. In such cases it is necessary to add a little pure methyl alcohol in order to redissolve the oil, otherwise the reduction of the ketone alcohol may be incomplete. A purer product is, however, obtained when the solu-

tion employed is so dilute that the addition of methyl alcohol becomes unnecessary, as in this case the oily bye-products which seem to be always formed in very small quantities can be subsequently separated by filtration. The slightly turbid aqueous solution is decanted from the mercury, saturated with carbonic anhydride, allowed to cool completely, and then filtered from the crystals of sodium hydrogen carbonate. The glycol in the clear solution is extracted by repeatedly shaking with pure ether, and the ethereal extract, after drying over potassium carbonate, is evaporated.

Phenylpentamethylene glycol is thus obtained in the form of a thick, colourless oil; when kept for some time over sulphuric acid under reduced pressure, it begins to crystallise, and on stirring the oil with a glass rod, it quickly solidifies to a hard, colourless, crystalline mass, a considerable development of heat taking place. The analysis of the crystalline compound gave the following result—

0·1935 gram of substance gave 0·5199 gram of CO_2 and 0·1614 gram of H_2O.

	Calculated for $C_{11}H_{16}O_2$.	Found.
C	73·33 per cent.	73·26 per cent.
H	8·89 „	9·26 „
O	17·78 „	17·48 „

Phenylpentamethylene glycol dissolves freely in hot benzene, and on cooling quickly it separates from the solution in an oily condition; if, however, a cold benzene solution is allowed to evaporate slowly at the ordinary temperature, the glycol separates in transparent, concentrically-grouped needles melting at about 54°. It is very readily soluble in cold ether, alcohol, and ethyl acetate, but only sparingly in hot light petroleum. It dissolves moderately easily in both hot and cold water, but on adding potassium carbonate to the solution, it is partially reprecipitated as an oil or in a crystalline condition. When heated in small quantities in a test tube under the ordinary pressure, it distils without leaving any residue, and water condenses on the cooler portions of the test tube; it is probable that on distillation the glycol is converted into an oxide of the constitution $CH_2<\begin{matrix}CH_2\cdot CHPh\\CH_2—CH_2\end{matrix}>O$.

Phenylpentamethylene glycol dissolves in concentrated hydrobromic acid, with development of heat, and is thereby partially converted into the bromide, which separates from the solution almost immediately in the form of a yellowish oil.

ω-Phenylpentamethylene Bromide, $C_6H_5 \cdot CHBr \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2Br$.

The only method by which phenylpentamethylene bromide can be easily prepared from the corresponding glycol seems to be to treat the glycol with phosphoric bromide in chloroform solution.

When the glycol is treated with concentrated hydrobromic acid, either in the cold or at a moderately high temperature, the product still contains a considerable quantity of the monobromide or unchanged glycol. In the first attempts to prepare the dibromide, the pure crystalline glycol was dissolved in twelve times its weight of the acid (saturated at 0°), the mixture shaken well and then heated on the water-bath for about two hours, with frequent shaking. The supernatant, dark-brown oil was then separated, dissolved in ether, the ethereal solution washed with a little dilute sodium carbonate, dried over calcium chloride, and evaporated. A bromine determination, made with a portion of this product which had been kept for 24 hours over sulphuric acid, gave the following result—

0·3018 gram of substance gave 0·2791 gram of silver bromide.

	Calculated for $C_{11}H_{14}Br_2$.	Found.
Br.....	52·27 per cent.	39·3 per cent.

As the analysis showed that the conversion into the dibromide was far from being complete, the crude product was again treated with hydrobromic acid exactly as described above, and the dark-brown oil analysed; the percentage of bromine had only increased to 44·6. As the failure of these experiments seemed to be due to the insolubility of the partially brominated oil in the acid, the next attempts to prepare the dibromide were carried out as follows:—The glycol, or the partially brominated compound, was dissolved in a large quantity of glacial acetic acid, the solution saturated with hydrogen bromide at 0°, and kept for three hours at the ordinary temperature. It was then largely diluted with water, the precipitated oil extracted with ether, and isolated in the usual way. This treatment gave no better results. In the last experiments which were made with hydrobromic acid, the following method was employed:—The crude bromide from a previous operation (containing 43·4 per cent. of bromine) was dissolved in about 20 volumes of glacial acetic acid, the solution saturated with hydrogen bromide at 0° and then heated at 110—120° for about eight hours in sealed tubes; the resulting dark-brown oil contained a slightly larger percentage of bromine, as is shown by the following analysis—

0·2032 gram of substance gave 0·2248 gram of silver bromide.

	Calculated for $C_{11}H_{14}Br_2$.	Found.
Br.....	52·27 per cent.	47·2 per cent.

This method not being considered satisfactory, and a purer product being required for subsequent experiments, the action of phosphorus tribromide on the glycol was investigated. The pure glycol was boiled for about an hour, in a flask provided with a reflux apparatus, with a considerable excess of phosphorus tribromide; the product obtained in this way contained about 44 per cent. of bromine, but considerable quantities of resinous substances are formed in the reaction; for this reason the yield is very unsatisfactory and the dibromide obtained is very impure.

The method of preparation finally adopted, and which gives an almost pure product in theoretical quantity, is the following:—The pure glycol is dissolved in about 30 times its weight of pure chloroform and a small quantity of phosphorus pentabromide added to the solution; a slight development of heat occurs and a copious evolution of hydrogen bromide commences at once. As soon as the action has ceased, the addition of the phosphorus pentabromide is continued, small portions being added from time to time until the amount employed is about twice the calculated quantity. After keeping the mixture for two days in a desiccator, the chloroform solution is decanted and the residual pentabromide washed with a little dry chloroform; the chloroform solutions are mixed together, washed with water, then with a little dilute sodium carbonate, and finally with water again, dried over calcium chloride, and the chloroform evaporated on the water-bath.

The dibromide is thus obtained in an almost pure condition in the form of a thick, almost colourless oil; bromine determinations were made with three different samples which had been kept for some time over paraffin under reduced pressure. The following are the results:—

I. 0·3416 gram of substance gave 0·4205 gram of silver bromide.
II. 0·1442 gram of substance gave 0·1750 gram of silver bromide.
III. 0·2338 gram of substance gave 0·2806 gram of silver bromide.

	Calculated for $C_{11}H_{14}Br_2$.	Found.		
		I.	II.	III.
Br.....	52·27 p. c.	50·3	51·7	51·2 p. c.

Phenylpentamethylene bromide is a thick, almost colourless oil with a pleasant, rather sweet smell; it is readily soluble in ether but only very sparingly in alcohol, and seemingly insoluble in water and in concentrated hydrobromic acid. When distilled over lime, it

yields small quantities of a colourless compound which has a strong odour of naphthalene and crystallises in colourless plates; the nature of this substance has not been determined owing to the small quantity at our disposal.

Phenylhexamethylenedicarboxylic acid,

$$CH_2<\begin{matrix}CH_2\cdot CHPh\\ CH_2-CH_2\end{matrix}>C(COOH)_2.$$

Ethyl phenylhexamethylenedicarboxylate is formed when ethyl malonate (2 mols.) is treated with phenylhexamethylene dibromide (1 mol.) and sodium ethoxide (2 mols.) in alcoholic ethereal solution; the reaction is represented by the equation—

$$C_6H_5\cdot CHBr\cdot[CH_2]_3\cdot CH_2Br + 2CHNa(COOEt)_2 = C_{14}H_{16}O_4 + CH_2(COOEt)_2 + 2NaBr.$$

This ethereal salt, on hydrolysis, yields phenylhexamethylenedicarboxylic acid.

Ethyl malonate (10·4 grams) is added in small portions at a time to a solution of sodium (1·5 grams) in about twelve times its weight of absolute alcohol, care being taken to prevent the temperature from rising above 35—40°. An ethereal solution of the dibromide (10 grams) is then added, and the mixture is heated on the water-bath in a flask provided with a reflux condenser; the addition of ether is necessary owing to the insolubility of the dibromide in alcohol. Just as the solution begins to boil, the separation of sodium bromide commences, and, after heating for about 1½ hours, the reaction is at an end. The alcohol is then distilled off, the residue treated with water to dissolve the sodium bromide, the oil extracted with ether, and the dried ethereal solution evaporated.

Ethyl phenylhexamethylenedicarboxylate,

$$CH_2<\begin{matrix}CH_2\cdot CHPh\\ CH_2-CH_2\end{matrix}>C(COOEt)_2,$$

is thus obtained in the form of a thick, yellowish-brown oil, which shows no signs of crystallisation even when kept for a long time over sulphuric acid under reduced pressure. This compound was not analysed and no attempts were made to obtain it in a pure condition; its method of formation and its decomposition into phenylhexamethylenedicarboxylic acid prove that it has the constitution given above.

Phenylhexamethylenedicarboxylic acid is produced when the ethereal salt just described is boiled for 4 to 5 hours with a concentrated alcoholic solution of potash. After distilling off the alcohol, the residue is treated with water, the aqueous solution evaporated in a

basin in order to expel the remainder of the alcohol, then diluted with water and filtered to free it from oily impurities. The filtrate is acidified with excess of dilute sulphuric acid, and the precip itated oil extracted with ether; on evaporating the dried ethereal solution, phenylhexamethylenedicarboxylic acid remains as a thick, yellow oil. No analysis of this compound was made owing to the difficulty of obtaining it in a pure condition; the fact that on heating it is converted into phenylhexamethylenecarboxylic acid, with evolution of carbonic anhydride, is sufficient proof that it has the formula assigned to it above.

Phenylhexamethylenecarboxylic acid, $CH_2<\begin{matrix}CH_2\cdot CHPh\\CH_2-CH_2\end{matrix}>CH\cdot COOH$.

Phenylhexamethylenecarboxylic acid can be obtained in two ways, as has been stated above; either by heating phenylhexamethylenedicarboxylic acid, or by the hydrolysis of ethyl phenylacetylhexamethylenecarboxylate.

The preparation of this compound from phenylhexamethylenedicarboxylic acid is carried out as follows:—The crude acid is placed in a small flat-bottomed flask and heated in a metal-bath at 150—160°, until the evolution of carbonic anhydride ceases; the temperature is then raised to 175—180°, and the heating continued for about 5 minutes in order to ensure complete decomposition. The residual dark-brown oil is transferred to a larger flask, and boiled for about an hour with excess of baryta; the monocarboxylic acid dissolves in the baryta, but a considerable quantity of dark-brown resinous products remain undissolved, and can be easily separated by filtration. The solution is then heated again to boiling, the excess of baryta precipitated with carbonic anhydride, the filtrate allowed to cool and treated with excess of dilute hydrochloric acid. The acid, which is precipitated as an oil, is extracted by repeatedly shaking with pure ether, and the ethereal solution dried over calcium chloride and evaporated.

The yellowish oil obtained in this way was kept over sulphuric acid under reduced pressure until its weight became constant, and then analysed with the following results:—

0·2983 gram of substance gave 0·7982 gram of CO_2 and 0·2120 gram of H_2O.

	Calculated for $C_{13}H_{16}O_2$.	Found.
C	76·47 per cent.	72·95 per cent.
H	7·84 „	7·93 „
O	15·69 „	19·12 „

The analysis having shown that the acid, purified in this way, still contains a considerable quantity of foreign substances, the oil was treated again with baryta exactly as described above, and then analysed.

0·2099 gram of substance gave 0·5644 gram of CO_2 and 0·1511 gram of H_2O.

	Calculated for $C_{13}H_{16}O_2$.	Found.
C	76·47 per cent.	73·76 per cent.
H	7·84 „	7·98 „
O	15·69 „	18·26 „

The analysis showed clearly that purification with baryta is of little use after the first treatment, so that other means had to be adopted to obtain the acid in a pure condition.

The method which invariably led to the best results was the following:—The yellow oil, obtained after treating once with baryta as described above, is mixed with a slight excess of very concentrated ammonia, and the mixture stirred well until the acid has completely dissolved; the solution is then transferred to a basin and kept in a desiccator over potassium carbonate, until the whole solidifies. The yellowish, waxy mass is spread on a porous plate and kept over potassium carbonate for a few days. The ammonium salt is thus obtained perfectly colourless and free from all oily impurities. It is dissolved in water, the solution acidified with excess of dilute sulphuric acid, and the oil extracted with pure ether. On evaporating the dried ethereal solution, there remains a thick, colourless oil, which after some time completely solidifies to a colourless crystalline mass.

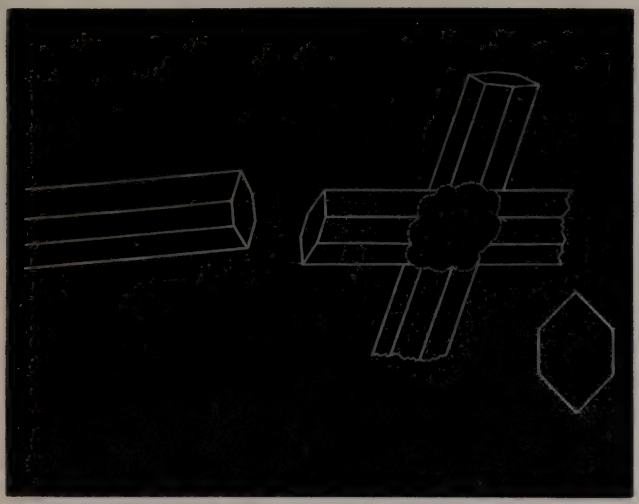
The analysis of the crystalline compound gave the following result:—

0·1637 gram of substance gave 0·4536 gram of CO_2, and 0·1201 gram of water.

	Calculated for $C_{13}H_{16}O_2$.	Found.
C	76·47 per cent.	75·57 per cent.
H	7·84 „	8·15 „
O	15·69 „	16·38 „

Phenylhexamethylenecarboxylic acid separates from warm light petroleum in beautiful, compact, rosette-shaped crystals; when crystallisation takes place slowly at the ordinary temperature, it separates from the solution in large, transparent, well-defined prisms. Some

of the crystals were drawn with the aid of the microscope and are shown in the diagram given below.



It melts at 104—105° and is readily soluble in cold ether, chloroform, methyl alcohol, acetone, and warm light petroleum, but only moderately in the cold solvent, and insoluble or very sparingly soluble in water. When heated in small quantities under the ordinary pressure, it distils with scarcely any decomposition and the distillate solidifies again on cooling; when the acid is heated quickly to a moderately high temperature, it gives off a pungent and irritating odour very like that of acraldehyde. It is only very slowly acted on by concentrated nitric acid; it is not oxidised by potassium permanganate in cold alkaline solution, but, on boiling, the pink colour of the solution gradually disappears.

The *silver* salt, $C_{13}H_{15}O_2Ag$, was prepared by precipitating a neutral aqueous solution of the ammonium salt with silver nitrate; the precipitate was washed with cold water, spread on a porous plate, and then dried for a short time at 100°.

A silver determination with the salt thus prepared gave the following result:—

0·2796 gram of the silver salt gave 0·0983 gram of silver.

	Calculated for $C_{13}H_{15}O_2Ag$.	Found.
Ag	34·66 per cent.	35·15 per cent.

Silver phenylhexamethylenecarboxylate is a colourless, seemingly

amorphous powder, only sparingly soluble in boiling water; on cooling the solution, the salt is deposited in waxy flakes. It seems to be fairly stable when exposed to light, and it is only after some hours that it acquires a slight pink tint in diffused sunlight. It can be heated at 100° for a short time without any appreciable decomposition taking place, but when heated more strongly it acquires a brilliant, green colour, and gives off vapours having an extremely disagreeable and pungent odour recalling that of burnt fat.

The *ammonium* salt can be obtained in the form of a colourless powder by dissolving the acid in concentrated ammonia and evaporating the solution at the ordinary temperature in an atmosphere of ammonia; it is very readily soluble in water.

In aqueous solutions of the ammonium salt, lead acetate, zinc sulphate, and mercurous nitrate produce colourless, amorphous precipitates, which are sparingly soluble in boiling water, and become soft and wax-like on heating. Ferric chloride produces a yellowish-brown precipitate which turns reddish-brown on warming, and is insoluble or only very sparingly soluble in boiling water. Copper sulphate gives a light-blue precipitate readily soluble in ammonia, and stannous chloride gives a colourless precipitate readily soluble in boiling water.

The salts of the alkaline earths and the magnesium salt are readily soluble in cold water, as even in moderately concentrated solutions of the ammonium salt, barium chloride, and magnesium chloride cause no precipitation.

Ethyl Phenylacetylhexamethylenecarboxylate,

$$CH_2<\begin{matrix}CH_2\cdot CHPh\\ CH_2-CH_2\end{matrix}>C<\begin{matrix}COMe\\ COOEt\end{matrix}.$$

Ethyl phenylacetylhexamethylenecarboxylate can be obtained by treating ethyl acetoacetate (1 mol.) with phenylpentamethylene bromide (1 mol.) and sodium ethoxide (2 mols.) in alcoholic solution; the reaction may be represented by the equation—

$$CH_3\cdot CO\cdot CH_2\cdot COOEt + C_6H_5\cdot CHBr\cdot[CH_2]_3\cdot CH_2Br + 2NaOC_2H_5 = C_6H_9Ph(CO\cdot CH_3)\cdot COOEt + 2NaBr + 2C_2H_5\cdot OH.$$

In preparing this compound, ethyl acetoacetate (6·5 grams) is gradually added to an alcoholic solution of sodium (1·2 grams) in small portions at a time, the mixture being cooled well under the tap during the operation. The phenylpentamethylene bromide (15·3 grams) dissolved in about 10 volumes of dry ether is then added, and the mixture is heated on the water-bath in a flask provided with a reflux condenser; as the solution begins to boil, a considerable quantity of

sodium bromide is deposited, and after heating for about half an hour the action is at an end. The flask is then cooled under the tap, a solution of sodium (1·2 grams) in absolute alcohol added in small portions at a time, the mixture being kept cold during the operation, and then the whole heated again on the water-bath for about two hours. The alcohol is then distilled, the residue treated with water, and the oily product extracted with ether; on evaporating the dried ethereal solution, the ethyl phenylacetylhexamethylenecarboxylate remains as a yellowish oil (14 grams). No attempts were made to obtain this compound in a pure condition, and no analysis was made; its constitution is, however, proved by its method of preparation and by its decomposition into phenylacetylhexamethylene and phenylhexamethylenecarboxylic acid as described below.

Phenylhexamethylene Methyl Ketone, $CH_2<\begin{matrix}CH_2\cdot CHPh\\CH_2-CH_2\end{matrix}>CH\cdot CO\cdot CH_3$.

When the crude ethyl phenylacetylhexamethylenecarboxylate, obtained as described above, is hydrolysed with alcoholic potash, it is converted into phenylhexamethylene methyl ketone(phenylacetylhexamethylene) and phenylhexamethylenecarboxylic acid, according to the equations—

$$C_6H_9Ph(COMe)\cdot COOC_2H_5 + 2KOH = C_6H_9Ph\cdot COMe + K_2CO_3 + C_2H_5\cdot OH.$$

$$C_6H_9Ph(COMe)\cdot COOC_2H_5 + 2KOH = C_6H_9Ph\cdot COOK + C_2H_3O_2K + C_2H_5\cdot OH.$$

The relative quantity of the two products depends to some extent on the manner in which the hydrolysis is carried out; if the whole of the alcoholic potash is added at once, and the mixture then boiled the yield of ketone is less and that of the acid larger than when the alcoholic potash is added in small quantities at a time to the hot solution of the ethereal salt.

The following method was found to give a good yield of ketone:—The ethereal salt (13 grams) is dissolved in a small quantity of alcohol, the solution heated to boiling on the water-bath, and then a concentrated aqueous alcoholic solution of potash (24 grams) gradually added through a dropping funnel; as soon as the whole of the potash has been added, the mixture is boiled for a few minutes, and the alcohol is then distilled off. On adding water to the residue, the ketone separates as an oil, and can be easily extracted by shaking with ether; the phenylhexamethylenecarboxylic acid remains as potassium salt in the alkaline solution, and can be isolated as described below.

On evaporating the dried ethereal solution, the ketone remains in the form of a brown, moderately mobile oil, the yield of the crude product being 6·5 grams from 13 grams of the ethereal salt. When this oil is submitted to fractional distillation under a pressure of 50 mm., the thermometer rises rapidly to about 190°, and almost the whole passes over between 196° and 203°; the fraction collected between 196° and 203° was fractionated again under a pressure of 40 mm., and the portion boiling constantly at 187—190° collected separately. On cooling, this fraction solidified to a mass of colourless crystals, which were spread on a porous plate to free them from traces of oil, and then analysed.

The following was the result of the analysis:—

0·1442 gram of substance gave 0·4358 gram of CO_2 and 0·1202 gram of H_2O.

	Calculated for $C_{14}H_{18}O$.	Found.
C	83·16 per cent.	82·42 per cent.
H.....	8·91 „	9·26 „
O	7·92 „	8·32 „

Phenylhexamethylene methyl ketone is a colourless, crystalline compound, with an odour recalling that of the higher homologues of acetophenone. It melts at about 78—79°, and boils at 187—190° under a pressure of 40 mm. It is readily soluble in ether, alcohol, benzene, chloroform, and most of the ordinary organic solvents, but insoluble or only very sparingly soluble in water. It separates from cold ether in long, feathery crystals, and on adding water to a cold methyl alcoholic solution it is precipitated in colourless needles.

Phenylhexamethylene Methyl Ketone Oxime,

$$CH_2<\begin{matrix}CH_2\cdot CHPh\\ CH_2-CH_2\end{matrix}>CH\cdot CMe{:}N\cdot OH.$$

The oxime was prepared by treating the pure ketone with a slight excess of hydroxylamine hydrochloride and a large excess of potash in cold, aqueous alcoholic solution. After keeping for about two days, the alcohol is evaporated on the water-bath, the residue dissolved in water, and the cold solution slightly acidified with dilute hydrochloric acid; the precipitated oil is extracted with pure ether the ethereal solution dried, filtered, and the ether evaporated.

The thick, almost colourless oil obtained in this way was kept for some time over sulphuric acid under reduced pressure, but it showed no signs of crystallising. A nitrogen determination was made and gave the following result:—

0·1158 gram of substance gave 6·6 c.c. of nitrogen, measured at 16° and 715 mm. pressure.

	Calculated for $C_{14}H_{19}NO$.	Found.
N	6·45 per cent.	6·55 per cent.

Phenylhexamethylene methyl ketone oxime is a thick, almost colourless oil, very sparingly soluble or insoluble in water, but readily soluble in ether, alcohol, and most ordinary organic solvents.

Phenylhexamethylenecarboxylic acid, $CH_2<\begin{matrix}CH_2\cdot CHPh\\CH_2-CH_2\end{matrix}>CH\cdot COOH$.

The alkaline solution obtained by the hydrolysis of ethyl phenylacetylhexamethylenecarboxylate contains the potassium salt of phenylhexamethylenecarboxylic acid, as has been stated above. After extracting the ketone with ether, the solution is acidified with dilute sulphuric acid, and the precipitated oil extracted with ether; about 5 grams of the crude acid is obtained in this way from 13 grams of the ethereal salt, and an analysis of this product gave the following result:—

0·1509 gram of substance gave 0·4030 gram of CO_2 and 0·1056 gram of H_2O.

	Calculated for $C_{13}H_{16}O_2$.	Found.
C	76·47 per cent.	72·83 per cent.
H.....	7·84 „	7·77 „
O.....	15·69 „	19·40 „

As the acid showed no signs of crystallisation, even when rubbed with a crystal of the substance obtained from phenylpentamethylene bromide and ethyl sodiomalonate, it was first purified by treating it with baryta as previously described. It was then dissolved in a little concentrated ammonia, the solution allowed to evaporate over potassium carbonate, and the residual ammonium salt spread on a plate to free it from small quantities of oily impurities. The salt was dissolved in dilute ammonia, the solution boiled with animal charcoal, filtered, and acidified with dilute sulphuric acid; the precipitated acid was then extracted with pure ether, and the dried ethereal solution evaporated.

The colourless oil obtained in this way soon solidified to a colourless, crystalline mass; after spreading on a porous plate and washing the crystals with a little light petroleum, they were analysed with the following result:—

0·1461 gram of substance gave 0·4078 gram of CO_2 and 1·1060 gram of H_2O.

	Calculated for $C_{13}H_{16}O_2$.	Found.
C	76·47 per cent.	76·12 per cent.
H.....	7·84 „	8·06 „
O	15·69 „	15·82 „

Phenylhexamethylenecarboxylic acid, prepared from ethyl acetoacetate, separates from light petroleum in crystals to all appearance identical with those of the acid obtained from ethyl malonate and phenylpentamethylene bromide. It has the same melting point (104—105°), shows a like behaviour with solvents, and gives the same precipitates with solutions of metallic salts.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Synthesis of Homologues of Pentanetetracarboxylic Acid and of Pimelic Acid.

By W. H. Perkin, Jun., Ph.D., F.R.S., and Bertram Prentice.

In a previous communication to the Society on derivatives of pentamethylene (Trans., 1887, **51**, 240), it was shown that ethyl pentanetetracarboxylate, $(COOC_2H_5)_2CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(COOC_2H_5)_2$, produced by the action of trimethylene bromide on the sodium derivative of ethyl malonate, was capable of forming a disodium compound, $(COOC_2H_5)_2CNa\cdot CH_2\cdot CH_2\cdot CH_2\cdot CNa(COOC_2H_5)_2$, which, when treated with bromine, yielded ethyl pentamethylenetetracarboxylate.

This disodium compound reacts readily also with methylene iodide, forming, among other products, ethyl hexamethylenetetracarboxylate, as is shown in the preceding paper.

In the course of these experiments, it appeared to us interesting to include the study of the action of alkyl iodides on the disodium compound of ethyl pentanetetracarboxylate, and as a result we find that this reaction serves as a very convenient method of preparing $\alpha\alpha$-disubstituted pentanetetracarboxylic acid derivatives, and, indirectly, of $\alpha\alpha$-disubstituted pimelic acids, thus :—

$$(COOC_2H_5)_2CNa\cdot CH_2\cdot CH_2\cdot CH_2\cdot CNa(COOC_2H_5)_2 + 2RI = (COOC_2H_5)_2CR\cdot CH_2\cdot CH_2\cdot CH_2\cdot CR(COOC_2H_5)_2 + 2NaI.$$

On hydrolysis, the ethereal salts thus obtained yield the corresponding tetrabasic acids, and these, when heated at 200—220°, are readily decomposed with evolution of 2 mols. of carbonic anhydride and formation of homologues of pimelic acid, thus :—

$$(COOH)_2CR\cdot CH_2\cdot CH_2\cdot CH_2\cdot CR(COOH)_2 = COOH\cdot CHR\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHR\cdot COOH + 2CO_2.$$

On the other hand, it was not found possible to prepare monalkyl

derivatives of pentanetetracarboxylic acid by treating ethyl pentanetetracarboxylate with 1 mol. of sodium ethylate and alkyl haloïds.

Thus, when benzyl chloride was employed, the product of the reaction was found to consist of ethyl dibenzylpentanetetracarboxylate, one half of the ethyl pentanetetracarboxylate being recovered as such. In order to explain this curious reaction, one must either suppose that ethyl pentanetetracarboxylate is incapable of forming a monosodium compound, under the conditions employed, or that the decomposition of the monosodium compound takes place thus:—

I. $(COOC_2H_5)_2CNa\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2 + C_7H_7Cl =$
$(COOC_2H_5)_2C(C_7H_7)\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2 + NaCl.$

II. $(COOC_2H_5)_2C(C_7H_7)\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2 +$
$(COOC_2H_5)_2CNa\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2 =$
$(COOC_2H_5)_2C(C_7H_7)\cdot[CH_2]_3\cdot CNa(COOC_2H_5)_2 +$
$(COOC_2H_5)_2CH\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2.$

III. $(COOC_2H_5)_2C(C_7H_7)\cdot[CH_2]_3\cdot CNa(COOC_2H_5)_2 + C_7H_7Cl =$
$(COOC_2H_5)_2C(C_7H_7)\cdot[CH_2]_3\cdot C(C_7H_7)(COOC_2H_5)_2 + NaCl.$

Similar results were obtained by Guthzeit and Dressel (*Annalen*, **256**, 180 and 188), who found that ethyl dicarboxyglutarate, $(COOC_2H_5)_2CH\cdot CH_2\cdot CH(COOC_2H_5)_2$, was apparently not capable of yielding a monosodium compound, and that, consequently, when the ethereal salt was treated with 1 mol. of sodium ethylate and ethyl iodide, instead of ethyl *mon*ethyldicarboxyglutarate, a mixture of ethyl *di*ethyldicarboxyglutarate with unchanged ethyl dicarboxyglutarate resulted.

Derivatives of ethyl pentanetetracarboxylate and of pimelic acid, identical with those obtained by the above method, may be conveniently prepared by acting on the sodium compound of the ethyl alkylmalonate with trimethylene bromide, thus:—

$2(COOC_2H_5)_2CRNa + C_3H_6Br_2 =$
$(COOC_2H_5)_2CR\cdot[CH_2]_3\cdot CR(COOC_2H_5)_2 + 2NaBr.$

The action of trimethylene bromide on the sodium compound of ethyl isobutylmalonate was carefully investigated, and it was found that nearly 50 per cent. of the theoretical yield of ethyl diisobutylpentanetetracarboxylate was obtained in this way; hence this method may, obviously, in many cases, be conveniently employed instead of that just described, especially as it is more expeditiously carried out.

The smallness of the yield of ethyl diisobutylpentanetetracarboxylate appears to be due to a secondary reaction, in which ethyl

isobutylallylmalonate is formed, with regeneration of some ethyl isobutylmalonate, thus :—

$$2(COOC_2H_5)_2CNa\cdot C_4H_9 + C_3H_6Br_2 = (COOC_2H_5)_2C(CH_2\cdot CH{:}CH_2)\cdot C_4H_9 + (COOC_2H_5)_2CH\cdot C_4H_9 + 2NaBr.$$

The study of the disubstituted pimelic acids is of considerable interest in view of the work lately done by Zelinsky, Auwers and Victor Meyer, Bischoff, and his collaborateurs, and others, on the stereochemical isomerism of $\alpha\alpha$-disubstituted acids in the succinic, glutaric, and adipic series.

The symmetrical disubstituted succinic acids, $\begin{matrix}CHX\cdot COOH\\ CHX\cdot COOH\end{matrix}$', exist in two modifications or so-called stereochemical isomerides which may be conveniently represented thus :—

$$\begin{matrix}X\cdot CH\cdot COOH\\ COOH\cdot HC\cdot X\end{matrix}\quad\text{(Fumaroïd form.)} \qquad \begin{matrix}X\cdot CH\cdot COOH\\ X\cdot CH\cdot COOH\end{matrix}\quad\text{(Maleïnoïd form.)}$$

Similarly, symmetrical dimethylglutaric acid,

$$CH_2{<}\begin{matrix}CH(CH_3)\cdot COOH\\ CH(CH_3)\cdot COOH\end{matrix}'$$

exists in two modifications; the corresponding diphenylglutaric acid has, on the contrary, only been obtained in one form.

Again, symmetrical dimethyladipic acid, $\begin{matrix}CH_2\cdot CH(CH_3)\cdot COOH\\ CH_2\cdot CH(CH_3)\cdot COOH\end{matrix}$' exists in the form of two stereochemical isomerides.

It naturally appeared to us interesting to determine whether the symmetrical $\alpha\alpha$-pimelic acids existed in two modifications, which, in the case of dimethylpimelic acid, would be represented by the formulæ

$$\begin{matrix}CH_3\cdot CH\cdot COOH\\ [CH_2]_3\\ COOH\cdot HC\cdot CH_3\end{matrix}\quad\text{(Fumaroïd form.)} \qquad \begin{matrix}CH_3\cdot CH\cdot COOH\\ [CH_2]_3\\ CH_3\cdot CH\cdot COOH\end{matrix}\quad\text{(Maleïnoïd form.)}$$

With this object in view, a considerable number of these di-substituted pimelic acids were prepared, and very carefully fractionally recrystallised from water, but in no case could a separation into two isomerides be accomplished. This investigation was, however, rendered very difficult from the fact that, unlike the disubstituted succinic acids, the acids of the pimelic series have little capacity for crystallising.

It was frequently noticed that the melting points of the acids were not so sharp as could have been desired, and there is, therefore, still a possibility that stereochemical isomerides exist, which, however, are so similar in properties that means other than simple recrystallisation would need to be resorted to in order to effect separation.

A curious result was obtained in studying the action of benzal chloride on the disodium compound of ethyl pentanetetracarboxylate. This experiment was instituted in the hope of obtaining phenylhexamethylene derivatives, thus:—

$$(COOC_2H_5)_2CNa\cdot[CH_2]_3\cdot CNa(COOC_2H_5)_2 + C_6H_5\cdot CHCl_2 = (COOC_2H_5)_2C<\begin{matrix}CH_2\cdot CH_2\cdot CH_2\\ CH(C_6H_5)\end{matrix}>C(COOC_2H_5)_2 + 2NaCl,$$

a reaction analogous to the formation of ethyl hexamethylenetetracarboxylate by the action of methylene iodide on the disodium compound of ethyl pentanetetracarboxylate (compare p. 803).

On hydrolysing the ethereal salt obtained in this reaction, a hexamethylenetetracarboxylic acid was not obtained, as was expected, but instead of this, an acid which on investigation proved to be dibenzalpimelic acid. The formation of this acid by the action of benzal chloride on the disodium compound of ethyl pentanetetracarboxylate and subsequent hydrolysis may be represented thus:—

$$2(COOC_2H_5)_2CNa\cdot[CH_2]_3\cdot CNa(COOC_2H_5)_2 + 2C_6H_5\cdot CHCl_2 + 10KOH = COOK\cdot C(CH\cdot C_6H_5)\cdot[CH_2]_3\cdot C(CH\cdot C_6H_5)\cdot COOK + (COOK)_2CH\cdot[CH_2]_3\cdot CH(COOK)_2 + 4NaCl + 8C_2H_5\cdot OH + 2K_2CO_3,$$

but the exact course of the reaction is difficult to explain.

It is, however, possible that, in the first place, an intermediate compound,

$$(COOC_2H_5)_2C(CHCl\cdot C_6H_5)\cdot[CH_2]_3\cdot C(CHCl\cdot C_6H_5)(COOC_2H_5)_2,$$

is formed, half of the sodium compound of ethyl pentanetetracarboxylate remaining unacted on. On subsequent hydrolysis, this intermediate substance would yield dibenzalpimelic acid, thus:—

$$(COOC_2H_5)_2(CHCl\cdot C_6H_5)C\cdot[CH_2]_3\cdot C(CHCl\cdot C_6H_5)(COOC_2H_5)_2 + 8KOH = COOK\cdot C(CH\cdot C_6H_5)\cdot[CH_2]_3\cdot C(CH\cdot C_6H_5)\cdot COOK + 2KCl + 4C_2H_5\cdot OH + 2K_2CO_3 + 2H_2O,$$

whilst the excess of ethyl pentanetetracarboxylate, on hydrolysis and subsequent heating at 200°, would yield pimelic acid; this was actually found as one of the products of the reaction.

Ethyl pentanetetracarboxylate is readily acted on by bromine with

formation of ethyl $\alpha\alpha$-dibromopentanetetracarboxylate and evolution of hydrogen bromide, thus:—

$$(COOC_2H_5)_2CH\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2 + 2Br_2 = (COOC_2H_5)_2CBr\cdot[CH_2]_3\cdot CBr(COOC_2H_5)_2 + 2HBr.$$

This dibromo-compound is remarkable for the ease with which it is converted into ethyl pentamethylenetetracarboxylate, this change taking place when the substance is treated with alcoholic potash or alcoholic ammonia, and apparently quantitatively when it is boiled in alcoholic solution with the sodium compound of ethyl malonate. It seems probable that this latter reaction takes place according to the equation

$$(COOC_2H_5)_2CBr\cdot CH_2\cdot CH_2\cdot CH_2\cdot CBr(COOC_2H_5)_2 + 2(COOC_2H_5)_2CHNa = \begin{matrix} & & CH_2\cdot CH_2\cdot CH_2 & & \\ & & | & | & \\ (COOC_2H_5)_2C & & & & C(COOC_2H_5)_2 \end{matrix} + (COOC_2H_5)_2CH\cdot CH(COOC_2H_5)_2 + 2NaBr,$$

a striking example of the tendency towards the formation of a pentamethylene ring; clearly by this reaction a hexamethylene ring might have been produced, thus:—

$$(COOC_2H_5)_2CBr\cdot CH_2\cdot CH_2\cdot CH_2\cdot CBr(COOC_2H_5)_2 + 2(COOC_2H_5)_2CHNa = \begin{matrix} & CH_2 & CH_2 & CH_2 & \\ & | & & | & \\ (COOC_2H_5)_2C & \cdot & C(COOC_2H_5)_2 & \cdot & C(COOC_2H_5)_2 \end{matrix} + (COOC_2H_5)_2CH_2 + 2NaBr,$$

and it would be a matter of considerable interest to determine whether by varying the conditions the hexamethylene compound could be obtained.

With regard to the descriptions of the properties of the substances obtained in this research, we wish to add that the density and magnetic rotation determinations were made by W. H. Perkin (sen.), who will, in a forthcoming paper, describe his observations in detail. We have also to express our thanks to Dr. J. Walker, to whom we are indebted for the determinations of the dissociation constants for the electrical conductivity of the pimelic acids.

Ethyl Pentanetetracarboxylate,

$(COOC_2H_5)_2CH\cdot[CH_2]_3\cdot CH(COOC_2H_5)_2$.

This substance has already been described (Trans., 1887, **41**, 240). In preparing large quantities of this ethereal salt, the following quantities are advantageously employed in one operation:—

Ethyl malonate	320 grams.
Trimethylene bromide	210 „
Sodium.....	46 „
Alcohol.....	500—550 grams.

The reaction which sets in after mixing these substances (Trans., **41**, 241) is at times very violent; it is, therefore, necessary to employ a large flask fitted with a long condenser, and resting on several folds of cloth, otherwise loss from frothing or from breakage due to bumping may result. The crude ethyl pentanetetracarboxylate obtained from the product of this reaction by the method previously recommended (*loc. cit.*) does not boil constantly; but it nevertheless appears to be a very fairly pure substance, and for synthetical purposes the fraction passing over between 255° and 275° (under a pressure of 100 mm.) was found to give excellent results. A sample of this ethereal salt boiling at 230—235° (30 mm.)* gave on analysis the following numbers—

0·1705 gram substance gave 0·1198 gram H_2O and 0·3350 gram CO_2.

	Theory. $C_{17}H_{28}O_8$.	Found.
C.....	56·67 per cent.	56·78 per cent.
H.....	7·78 „	7·81 „
O.....	35·55 „	35·41 „

The boiling point of this ethereal salt was previously given as 259—262° (100 mm.), and this agrees well with that given above, that is, 230—235° (30 mm.).

Records of the yields obtained in a large number of experiments on the action of trimethylene bromide on the sodium compound of ethyl malonate have been kept, and the following may be given as approximately representing the proportion of the various products obtained from 1 kilo. of ethyl malonate.

Crude product of the reaction.....		1050—1090 grams.
After distillation in steam	crude ethyl tetramethylenedicarboxylate	570— 620 „
	crude ethyl pentanetetracarboxylate	420— 470 „
Ethyl pentanetetracarboxylate, b. p. 255—275° (100 mm.)		360— 390 „

* All boiling points given in this paper are to be understood as being taken with the thread of the thermometer immersed entirely in the vapour of the boiling liquid.

Pentanetetracarboxylic Acid, $(COOH)_2CH\cdot[CH_2]_3\cdot CH(COOH)_2$.

In the previous communication (*loc. cit.*), this acid was only obtained in a crude state, and was not then examined and analysed; it may be prepared in an approximately pure state in the following way:—

9 grams of the pure ethereal salt are gradually added to a moderately concentrated solution of 10 grams of pure potassium hydrate in methyl alcohol, and the mixture heated to boiling in a reflux apparatus for two hours. The product is evaporated, mixed with water, again evaporated to a small bulk to remove the last traces of alcohol, acidified with dilute sulphuric acid, and extracted at least 20 times with pure ether which must be quite free from alcohol. The ethereal solution is very carefully dried over calcium chloride, filtered, evaporated, and the residual oily acid allowed to stand several days over sulphuric acid in a vacuum.

In this way a crystalline cake is obtained, which after being freed, as far as possible, from oily mother liquor by spreading on a porous plate, is washed rapidly with a small quantity of pure ether on a piece of porous tile, and the residual white, crystalline mass dried over sulphuric acid in a vacuum. When analysed, it gave the following result:—

0·1396 gram substance gave 0·0667 gram H_2O and 0·2239 gram CO_2.

	Theory. $C_9H_{12}O_8$.	Found.
C	43·55 per cent.	43·74 per cent.
H.	4·84 ,,	5·30 ,,
O.....	51·61 ,,	50·96 ,,

Pentanetetracarboxylic acid begins to melt at 125—130°, and gradually decomposes with evolution of carbonic anhydride and formation of pimelic acid, thus:—

$$(COOH)_2CH\cdot[CH_2]_3\cdot CH(COOH)_2 = 2CO_2 + COOH\cdot CH_2\cdot[CH_2]_3\cdot CH_2\cdot COOH.$$

It is excessively soluble in water or alcohol, readily in ether, but almost insoluble in benzene and light petroleum.

The basicity of the acid was determined by titrating a known quantity with standard potassium hydrate solution.

0·5662 gram acid required for neutralisation 88·5 c.c. of standard solution of potassium hydrate (1 c.c. = 0·00559 gram KOH) = 0·492 gram KOH.

A tetrabasic acid of the formula $C_9H_{12}O_8$ requires = 0·511 gram KOH.

The results of the analysis and the titration of this acid seem to show that it contains a small quantity of pentanetricarboxylic acid.

Preparation of Ethyl Pimelate and Pimelic Acid.

The fact that pentanetetracarboxylic acid, on heating, is decomposed into pimelic acid and carbonic anhydride affords a valuable method for the preparation of this acid: more especially as other methods of preparation leave some doubt as to the normal structure of the resulting acid. We have had occasion to prepare a quantity of pimelic acid, and have found the following method, which differs from that previously given (Trans., 1887, **51**, 242), to give admirable results:—

Crude ethyl pentanetetracarboxylate (which need not be submitted to fractionation in a vacuum) is hydrolysed by boiling with an alcoholic solution of $1\frac{1}{2}$ times the theoretical quantity of potassium hydrate for 2 to 3 hours in a reflux apparatus, the alcohol driven off on a water-bath, and the residue dissolved in water and boiled vigorously to remove the last traces of alcohol. The concentrated solution is acidified with an excess of dilute sulphuric acid, and extracted about 20 times with pure ether; the extract is then dried over calcium chloride, evaporated, and the residual crude pentanetetracarboxylic acid heated in an oil-bath at about 200—220° until the evolution of carbonic anhydride has ceased. The crude, dark-coloured pimelic acid thus obtained is best purified by conversion into its ethereal salt; for this purpose, the crude product is dissolved in about 6 times its weight of absolute alcohol, about one-fifth of the volume of concentrated sulphuric acid added, and the whole heated to boiling in a reflux apparatus for two hours. The alcoholic solution is then poured into much water, extracted four times with ether, and the ethereal solution washed twice with water and once with dilute sodium carbonate solution; the ethereal solution, after being dried over potassium carbonate, is evaporated, and the residual, brownish-coloured oil purified by distillation under reduced pressure (100 mm.). After two fractionations, nearly the whole of it passed over between 192° and 194° (under a pressure of 100 mm.), and gave, on analysis, the following numbers:—

0·1054 gram substance gave 0·0891 gram H_2O and 0·2360 gram CO_2.

	Theory. $COOC_2H_5\cdot[CH_2]_5\cdot COOC_2H_5$.	Found.
C	61·11 per cent.	61·06 per cent.
H	9·26 „	9·38 „
O	29·63 „	29·46 „

Ethyl pimelate is a colourless, limpid oil, which has a penetrating odour, somewhat resembling that of ethyl succinate. The density of this ethereal salt was found to be $d\,4°/4° = 1·0080$; $d\,15°/15° = 0·9988$; $d\,25°/25° = 0·9920$.

The magnetic rotation determinations gave—

t.	Sp. rotation.	Mol. rotation.
18·9°	0·9481	11·424

The acid was obtained from the ethereal salt by digesting it with excess of alcoholic potassium hydrate, evaporating the solution with the addition of water until free from alcohol, acidifying with dilute sulphuric acid, and extracting several times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a colourless oil which soon solidified to a hard, crystalline cake of almost pure pimelic acid; this was readily purified by conversion into the characteristic calcium salt (Dale, Schorlemmer, *Annalen*, **199**, 147) and subsequent recrystallisation from benzene. The beautiful product thus obtained gave on analysis:—

0·1202 gram substance gave 0·0828 gram H_2O and 0·2313 gram CO_2.

	Theory. $COOH\cdot[CH_2]_5\cdot COOH$.	Found.
C	52·50 per cent.	52·48 per cent.
H	7·50 „	7·65 „
O	40·00 „	39·87 „

The yield of pure pimelic acid obtained in this way from 180 grams of crude ethyl pentanetetracarboxylate was about 47 grams; the theoretical being 80 grams.

In a subsequent experiment made with the pure ethereal salt, the yield of recrystallised acid obtained was over 80 per cent. of the theory. The dissociation constant for the electrical conductivity of pimelic acid at different concentrations is K = 0·00341 (Ostwald gives 0·00357).

Pimelic acid is readily soluble in water.* 100 parts of water dissolve about 2·52 parts of pimelic acid at 13·5°.

* The determinations of the solubility of pimelic acid and its homologues which are given in this paper were made simultaneously; the acids were dissolved in

Ethyl Dibromopentanetetracarboxylate,

$(COOC_2H_5)_2CBr{\cdot}[CH_2]_3{\cdot}CBr(COOC_2H_5)_2$.

Ethyl pentanetetracarboxylate is very readily attacked by bromine at ordinary temperatures, and, if the addition of bromine is continued as long as decolorisation takes place, ethyl dibromopentanetetracarboxylate is formed, thus:—

$$(COOC_2H_5)_2CH{\cdot}[CH_2]_3{\cdot}CH(COOC_2H_5)_2 + 2Br_2 = (COOC_2H_5)_2CBr{\cdot}[CH_2]_3{\cdot}CBr(COOC_2H_5)_2 + 2HB$$

The following method answers well for preparing considerable quantities of this substance:—

36 grams of pure ethyl pentanetetracarboxylate is dissolved in 100 grams of pure dry chloroform, and 32 grams of bromine added very slowly and drop by drop through a dropping funnel; the mixture should be cooled during the operation by a stream of water, although the rise of temperature due to the reaction is not considerable. Each drop of bromine, as it comes in contact with the solution of the ethereal salt, is instantly decolorised, until about 28—30 grams have been added; then the reaction becomes very slow, and the liquid does not become colourless even on long standing.

The product thus obtained is washed twice with water, then with dilute sodium hydrate solution, and again with water; after being dried over calcium chloride, the chloroform is removed by allowing the solution to evaporate at a gentle heat on a water-bath, the last traces of chloroform being expelled by a current of air. The thick, oily residue, on cooling, soon begins to solidify, and if the crystallisation takes place slowly, large, well-formed, four-sided, tabular crystals, with bevelled edges, separate, and continue to grow until the whole mass has become solid. This crystalline mass was carefully pressed, dried over sulphuric acid in a vacuum, and analysed with the following result:—

0·1501 gram substance gave 0·0736 gram H_2O and 0·2140 gram CO_2.

0·2331 gram substance, heated with nitric acid and nitrate of silver in a sealed tube, gave 0·1684 gram AgBr.

	Theory. $C_{17}H_{26}Br_2O_8$.	Found.
C	39·38 per cent.	39·48 per cent.
H	5·02 ,,	5·44 ,,
Br	30·89 ,,	31·15 ,,

warm water, the solutions allowed to stand for two days to crystallise, filtered, and the amount of acid contained in the solutions estimated by titration.

Ethyl dibromopentanetetracarboxylate melts at about 38—40°. It is very readily soluble in most organic solvents; in cold light petroleum, however, it is only moderately soluble. We were not successful in our attempts to recrystallise the substance from any of these solvents.

Ethyl dibromopentanetetracarboxylate is readily hydrolysed by boiling with a mixture of dilute sulphuric acid and acetic acid, with formation of a crystalline acid, which appears to be dibromopentanetetracarboxylic acid. Alcoholic potash converts the dibromo-ethereal salt into pentamethylenetetracarboxylic acid, and the same remarkable change takes place, at all events to a small extent, when the ethereal salt is heated with alcoholic ammonia in a sealed tube. Similar results were obtained in experimenting on the action of ethyl dibromopentanetetracarboxylate on the sodium compound of ethyl malonate.

It seemed possible that this reaction might lead to a synthesis of hexamethylene derivatives (as explained in the introduction), and in order to submit this view to the test of experiment we proceeded as follows:—

3·3 grams of sodium was dissolved in 35 grams of absolute alcohol, the solution of sodium ethylate thus formed diluted with 50 c.c. of pure dry ether, and then 11·5 grams of ethyl malonate and 37 grams of ethyl dibromopentanetetracarboxylate added. After standing for half an hour, the product, which was quite neutral, was mixed with water, extracted two or three times with ether, the ethereal solution evaporated, and the residual thick oil hydrolysed by boiling it in a reflux apparatus for two days, with a mixture of 1 vol. of concentrated sulphuric acid, 1 vol. of water, and 2 vols. of glacial acetic acid. Steam was then blown through the mixture until all traces of acetic acid had been expelled, the slightly brownish liquid was filtered, allowed to stand for 24 hours, and the crystalline precipitate which had formed collected, washed with water, and recrystallised twice from this solvent.

Thus purified, the acid melted at 160°, and consisted of pure pentamethylenedicarboxylic acid. Analysis gave the following result:—

0·1510 gram substance gave 0·0868 gram H_2O and 0·2952 gram CO_2.

	Theory. $CH_2<^{CH_2\cdot CH\cdot COOH}_{CH_2\cdot CH\cdot COOH}$	Found.
C	53·16 per cent.	53·31 per cent.
H	6·33 „	6·38 „
O	40·51 „	40·31 „

The yield of the acid obtained in this experiment was very large,

and this method of preparation may possibly prove to be the simplest means of obtaining large quantities of pentamethylenedicarboxylic acid. Further experiments on this subject are in progress.

Ethyl Dimethylpentanetetracarboxylate,

$(COOC_2H_5)_2C(CH_3)\cdot[CH_2]_3\cdot C(CH_3)(COOC_2H_5)_2$.

As the methods employed in preparing the various homologues of ethyl pentanetetracarboxylate were in all cases very similar, we propose to give one example in full, and then in the other preparations simply to refer to this, giving only such important details as may be necessary.

In preparing ethyl dimethylpentanetetracarboxylate, 4·6 grams of sodium was dissolved in 50—55 grams of absolute alcohol, the well-cooled solution mixed with 36 grams of ethyl pentanetetracarboxylate (b. p. 255—275° at 100 mm.), and then an excess of methyl iodide (35 grams) added. The latter must be cautiously added, and with constant cooling, otherwise the reaction is apt to become very violent, and loss by boiling over may occur. The mixture was transferred to a soda-water bottle, heated in a water-bath at 100° for an hour, the product mixed with water, and the oily layer which separated extracted three times with ether. The ethereal solution was well washed with water, dried over calcium chloride, evaporated, and the almost colourless, oily residue purified by fractionation under reduced pressure (30 mm.). Almost the whole distilled between 235° and 245°, and on refractionation the ethereal salt was readily obtained pure as a thick oil boiling constantly at 238—240° (30 mm.).

The analysis gave the following result:—

0·1930 gram substance gave 0·1450 gram H_2O and 0·4148 gram CO_2.

	Theory. $C_{19}H_{32}O_8$.	Found.
C	58·76 per cent.	58·61 per cent.
H	8·25 „	8·34 „
O	32·99 „	33·05 „

Ethyl dimethylpentanetetracarboxylate is a thick, colourless oil possessing a feebly ethereal odour, and boiling constantly at 238—240° (30 mm.). It is insoluble in water, but miscible with alcohol, ether, and most organic solvents.

Dimethylpentanetetracarboxylic Acid,

$(COOH)_2C(CH_3)\cdot[CH_2]_3\cdot C(CH_3)(COOH)_2$.

In order to prepare this acid, the pure ethereal salt (1 mol.) was digested with an excess of a solution of pure potassium hydrate (6 mols.) in methyl alcohol for two hours in a flask connected with a reflux apparatus. The product was evaporated nearly to dryness, mixed with a considerable quantity of water, the solution again evaporated to a small bulk to remove the last traces of alcohol, acidified with dilute sulphuric acid, and extracted about 10 times with pure ether. The ethereal solution, after drying over calcium chloride, deposits during evaporation a white, sandy precipitate which consists of pure dimethylpentanetetracarboxylic acid. This was collected, washed with ether till quite colourless, dried over sulphuric acid in a vacuum, and analysed with the following results:—

I. 0·1555 gram substance gave 0·0830 gram H_2O and 0·2742 gram CO_2.

II. 0·1520 gram substance gave 0·0826 gram H_2O and 0·2698 gram CO_2.

	Theory. $C_{11}H_{16}O_8$.	Found. I.	Found. II.
C.....	47·83 per cent.	48·09	48·40 per cent.
H.....	5·79 „	5·93	6·03 „
O.....	46·37 „	45·98	45·57 „

The ethereal mother liquors from this acid on evaporation deposit a less pure acid, which was used in the subsequent preparation of dimethylpimelic acid.

Dimethylpentanetetracarboxylic acid, when rapidly heated, decomposes at about 200—205° into carbonic anhydride and dimethylpimelic acid. It is very soluble in water and alcohol, sparingly so in ether, benzene, light petroleum, chloroform, and ethyl acetate. Its aqueous solution has a strongly acid reaction. The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·1590 gram substance required for neutralisation 0·1285 gram KOH.

A tetrabasic acid of the formula $C_{11}H_{16}O_8$ requires 0·1289 gram KOH.

Ethyl Dimethylpimelate and Dimethylpimelic Acid,

$$COOH{\cdot}CH(CH_3){\cdot}[CH_2]_3{\cdot}CH(CH_3){\cdot}COOH.$$

When heated at 200°, dimethylpentanetetracarboxylic acid is rapidly decomposed with evolution of carbonic anhydride and formation of dimethylpimelic acid :—

$$(COOH)_2C(CH_3){\cdot}[CH_2]_3{\cdot}C(CH_3)(COOH)_2 = COOH{\cdot}CH(CH_3){\cdot}[CH_2]_3{\cdot}CH(CH_3){\cdot}COOH + 2CO_2.$$

The preparation and purification of this acid is readily accomplished in the following way :—

The crude tetrabasic acid, obtained as described in the previous section, is gradually heated in an oil-bath to 200°, and kept at this temperature until the evolution of carbonic anhydride ceases, the temperature being ultimately raised to 220° for one or two minutes. The crude, brownish-coloured acid is dissolved in absolute alcohol, digested with sulphuric acid, and thus converted into the diethyl salt, which is isolated and purified exactly as described under ethyl pimelate (p. 825).

Ethyl dimethylpimelate boils constantly at 195—196° (100 mm.), and in its properties closely resembles ethyl pimelate.

The analysis gave the following numbers :—

I. 0·1438 gram substance gave 0·1288 gram H_2O and 0·3352 gram CO_2.

II. 0·1270 gram substance gave 0·1132 gram H_2O and 0·2974 gram CO_2.

	Theory. $C_{13}H_{24}O_4$.	Found. I.	Found. II.
C	63·93 per cent.	63·85	63·86 per cent.
H	9·83 „	9·95	9·90 „
O	26·24 „	26·20	26·24 „

The specific gravity of ethyl dimethylpimelate is $d\ 4°/4° = 0·9817$; $d\ 15°/15° = 0·9728$; $d\ 25°/25° = 0·9663$.

The magnetic rotation determinations gave as an average—

t.	Sp. rotation.	Mol. rotation.
17·6°	0·9526	13·298

This ethereal salt is identical with the ethyl dimethylpimelate obtained by Kipping and Mackenzie (this vol., p. 571) by the action of trimethylene bromide on the sodium compound of ethyl methylacetoacetate. The boiling point given by these authors (190—191° under a pressure of 80 mm.) agrees well with that observed by us.

The preparation of *dimethylpimelic acid* from its ethereal salt is exactly similar to the preparation of pimelic acid from ethyl pimelate (p. 826).

The ethereal solution of the acid, on evaporation, deposited a thick oil which solidified when allowed to stand over sulphuric acid in a vacuum. The crystalline cake thus obtained was strongly pressed, and then purified by recrystallisation from water. This operation can be successfully carried out by dissolving the acid in sufficient hot water to allow of only a small quantity of oil separating on cooling. After standing for some days, beautiful, glistening, prismatic crystals grew from the oily drops; these were collected, washed with a little water, dried first on a piece of porous plate over sulphuric acid in a vacuum, then at 50—60°, and analysed (I). The mother liquors from these crystals, on standing over sulphuric acid in a vacuum, gradually deposited magnificent, glistening prisms, arranged in stellate groups: these were also collected and analysed (II).

I. 0·1460 gram substance gave 0·1132 gram H_2O and 0·3062 gram CO_2.

II. 0·1453 gram substance gave 0·1157 gram H_2O and 0·3060 gram CO_2.

	Theory. $C_9H_{16}O_4$.	Found. I.	Found. II.
C	57·44 per cent.	57·19	57·43 per cent.
H	8·51 „	8·61	8·84 „
O	34·05 „	34·20	33·73 „

Dimethylpimelic acid melts at 74—76°.

The dissociation constant for the electrical conductivity of this acid at different concentrations is K = 0·00337.

Dimethylpimelic acid has already been obtained by Kipping and Mackenzie (this vol., p. 570), by the hydrolysis of ethyl dimethyldiacetylpimelate, thus:—

$$\begin{matrix} CH_3CO \\ COOC_2H_5 \end{matrix}\!\!>\!C(CH_3)\cdot[CH_2]_3\cdot C(CH_3)\!<\!\begin{matrix} COCH_3 \\ COOC_2H_5 \end{matrix} + 4KOH =$$
$$COOK\cdot CH(CH_3)\cdot[CH_2]_3\cdot CH(CH_3)\cdot COOK + 2C_2H_3O_2K + 2C_2H_5\cdot OH.$$

These authors recrystallised their acid from a mixture of benzene and light petroleum, and obtained crystals melting at 81°.

We have also repeatedly recrystallised our acid from these solvents, but have never been able to observe a higher melting point than 74—76°.

Dimethylpimelic acid is readily soluble in water; 100 parts of water at 13·5° dissolve about 2·19 parts of the pure acid; but this

number must be regarded as approximate only, since this acid does not crystallise from water so readily as the other pimelic acids.

Ethyl Diethylpentanetetracarboxylate,

$(COOC_2H_5)_2C(C_2H_5)\cdot[CH_2]_3\cdot C(C_2H_5)\cdot(COOC_2H_5)_2$.

The quantities employed in preparing this compound were :—

Ethyl pentanetetracarboxylate.....	36·0 grams.
Sodium.....	4·6 „
Alcohol	55·0 „
Ethyl iodide	40·0 „

The operation was carried out exactly as described under ethyl dimethylpentanetetracarboxylate (p. 829); as, however, the reaction was not so energetic, the mixture was heated for two hours at 100°. The crude ethereal salt obtained weighed 40 grams, and, on fractionation, distilled, with the exception of very small high and low boiling fractions, between 245° and 250° (30 mm.). The pure substance boils constantly at 247° under a pressure of 30 mm. Analysis gave the following results :—

0·1640 gram substance gave 0·1300 gram H_2O and 0·3650 gram CO_2.

	Theory. $C_{21}H_{36}O_8$.	Found.
C	60·57 per cent.	60·69 per cent.
H	8·65 „	8·80 „
O	30·77 „	30·51 „

Ethyl diethylpentanetetracarboxylate is a thick, colourless oil boiling at 247° (30 mm.).

Diethylpentanetetracarboxylic Acid,

$(COOH)_2C(C_2H_5)\cdot[CH_2]_3\cdot C(C_2H_5)(COOH)_2$.

The hydrolysis of ethyl diethylpentanetetracarboxylate was conducted as described under dimethylpentanetetracarboxylic acid (p. 830). The ethereal solution of the tetrabasic acid was evaporated to a small bulk, allowed to stand, and the crystals which separated collected, washed rapidly with small quantities of pure ether on a filter pump, and dried over sulphuric acid in a vacuum.

The analysis gave the following result :—

0·1553 gram substance gave 0·0957 gram H_2O and 0·2930 gram CO_2.

	Theory. $C_{13}H_{20}O_8$.	Found.
C	51·31 per cent.	51·46 per cent.
H	6·58 „	6·84 „
O	42·11 „	41·70 „

Diethylpentanetetracarboxylic acid is a colourless, crystalline substance which, when heated in a capillary tube, decomposes at about 192—195° with evolution of carbonic anhydride and formation of diethylpimelic acid. It is very readily soluble in water and alcohol, and much more so in ether than the corresponding dimethyl acid, sparingly in benzene :—

The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·1536 gram substance required for neutralisation 0·1118 gram KOH.

A tetrabasic acid of the formula $C_{13}H_{20}O_8$ requires 0·1131 gram KOH.

Silver Diethylpentanetetracarboxylate, $C_{13}H_{16}Ag_4O_8$.—This salt was prepared from the neutral solution of the potassium salt by the addition of silver nitrate solution. The white, insoluble precipitate was collected, washed with water, dried over sulphuric acid in a vacuum, and analysed, with the following result :—

0·2834 gram substance gave on ignition 0·1659 gram silver.

	Theory. $C_{13}H_{16}Ag_4O_8$.	Found.
Ag.....	58·90 per cent.	58·54 per cent.

This silver salt is very stable and not readily acted on by light.

Ethyl Diethylpimelate and Diethylpimelic Acid,

$COOH{\cdot}CH(C_2H_5){\cdot}[CH_2]_3{\cdot}CH(C_2H_5){\cdot}COOH$.

Diethylpimelic acid was prepared by heating crude diethylpentanetetracarboxylic acid at 210—220° until the evolution of carbonic anhydride had ceased and then purifying the crude product by conversion into the diethyl salt (see p. 825). Ethyl diethylpimelate is a colourless, agreeably smelling oil which boils constantly at 209—211° (100 mm.).

Analysis :—

0·1317 gram substance gave 0·1222 gram H_2O and 0·3190 gram CO_2.

	Theory. $C_{15}H_{28}O_4$.	Found.
C	66·18 per cent.	66·06 per cent.
H.....	10·29 „	10·31 „
O	23·53 „	23·63 „

The specific gravity of this ethereal salt is $d\,4°/4° = 0·9667$; $d\,15°/15° = 0·9583$; $d\,25°/25° = 0·9509$.

The magnetic rotation determinations gave as an average :—

t.	Sp. rotation.	Mol. rotation.
18·2°	0·9708	15·355

Diethylpimelic acid was prepared from the pure ethereal salt by hydrolysis with alcoholic potassium hydrate (see p. 826). The alkaline solution of the potassium salt, deposits the acid, on acidifying, as a semi-solid mass; this was extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the residual solid acid purified by spreading on a porous plate and subsequently recrystallising it from water.

For analysis, the substance was dried over sulphuric acid in a vacuum :—

0·1508 gram substance gave 0·1254 gram H_2O and 0·3362 gram CO_2.

	Theory. $C_{11}H_{20}O_4$.	Found.
C	61·11 per cent.	60·80 per cent.
H	9·26 „	9·24 „
O.....	29·63 „	29·96 „

Diethylpimelic acid crystallises from water in four-sided prisms which resemble crystals of cane sugar in appearance and melt at 96—97°.

Diethylpimelic acid is sparingly soluble in cold water, about 0·234 part in 100 parts of water at 13·5°.

The basicity of this acid was determined by titration with normal potassium hydrate solution :—

0·1710 gram acid required for neutralisation 0·0883 gram KOH.

A bibasic acid of the formula $C_{11}H_{20}O_4$ requires 0·0889 gram KOH.

The dissociation constant for the electrical conductivity of diethylpimelic acid at different concentrations is $K = 0·00345$.

Ethyl Dipropylpentanetetracarboxylate,

$(COOC_2H_5)_2C(C_3H_7)\cdot[CH_2]_3\cdot C(C_3H_7)(COOC_2H_5)_2$.

The quantities used in the preparation of this substance were :—

Ethyl pentanetetracarboxylate ...	36·0 grams.
Sodium	4·6 „
Alcohol	60·0 „
Propyl iodide.....	40·0 „

the operation being conducted exactly as described under ethyl dimethylpentanetetracarboxylate. In this instance, however, on mixing the propyl iodide with the alcoholic solution of the disodium salt of ethylic pentanetetracarboxylate, only a slight evolution of heat was observable even after standing for some minutes. The product of the reaction was a thick oil, which, on twice fractioning, boiled constantly at 253—256° (30 mm.) as a colourless oil, which on standing completely solidified.

The crystalline cake was well pressed, dried over sulphuric acid in a vacuum and analysed with the following result :—

0·1583 gram substance gave 0·1290 gram H_2O and 0·3586 gram CO_2.

	Theory. $C_{23}H_{40}O_8$.	Found.
C	62·16 per cent.	61·77 per cent.
H	9·00 „	9·05 „
O	28·83 „	29·18 „

Ethyl dipropylpentanetetracarboxylate melts at about 52—54° and distils at 253—256° (30 mm.) ; it is very readily soluble in the usual organic solvents.

This ethereal salt gave somewhat curious results on hydrolysis ; this was conducted as usual (p. 830), and the resulting syrupy tetrabasic acid, which on standing became completely solid, was freed from traces of oily matter by spreading on a porous plate, and analysed with the following result :—

0·1596 gram substance gave 0·1194 gram H_2O and 0·3278 gram CO_2.

	Theory. $(COOH)_2C(C_3H_7)\cdot[CH_2]_3\cdot C(C_3H_7)(COOH)_2$.	Found.
C	54·21 per cent.	56·01 per cent.
H	7·23 „	8·31 „
O	38·56 „	35·68 „

The acid was then dissolved in a small quantity of warm water,

filtered, and the solution allowed to stand, when, in a short time, beautiful, four-sided, glistening plates separated; these were collected, washed with a little water, dried on a porous plate over sulphuric acid in a vacuum, and again analysed.

I. 0·1460 gram substance gave 0·1090 gram H_2O and 0·2990 gram CO_2.

II. 0·1433 gram substance gave 0·1075 gram H_2O and 0·2932 gram CO_2.

	Found.	
	I.	II.
C	55·85	55·80 per cent.
H	8·30	8·34 „

From these analytical results, this beautiful substance appears to be a mixture, in molecular proportion, of dipropylpentanetetracarboxylic acid and dipropylpentanetricarboxylic acid,

$$(COOH)_2C(C_3H_7)\cdot[CH_2]_3\cdot CH(C_3H_7)\cdot COOH;$$

such a mixture contains C = 56·13, H = 7·75 per cent. As, however, the crystals, when critically examined under the microscope, were found to be perfectly homogeneous, it appears probable that these two acids crystallise together in molecular proportion. The composition of these crystals is well borne out by the results obtained by titrating their aqueous solution with standard potassium hydrate solution; the numbers agree again with those required for a mixture of molecular proportions of the tribasic and tetrabasic acids.

0·1640 gram substance required for neutralisation 0·0964 gram KOH.

The mixture of tri- and tetra-basic acids requires 0·1037 gram KOH.

When heated in a capillary tube, these crystals decompose at 168° with evolution of carbonic anhydride and formation of dipropylpimelic acid.

Ethyl Dipropylpimelate and Dipropylpimelic Acid,

$$COOH\cdot CH(C_3H_7)\cdot[CH_2]_3\cdot CH(C_3H_7)\cdot COOH.$$

The crude acid obtained by the hydrolysis of ethyl dipropylpentanetetracarboxylate was heated in an oil-bath at 200—220°, till all evolution of carbonic anhydride had ceased, and the resulting thick, oily acid converted into the ethyl salt by means of alcohol and sulphuric acid (see p. 825). In this case it was found necessary to fraction the ethereal salt several times before it could be obtained pure.

Ethyl dipropylpimelate boils at 224—226° (100 mm.); it is a moderately thick oil of peculiar odour, closely resembling, though fainter than, that of ethyl pimelate. The analysis gave the following numbers:—

0·1484 gram substance gave 0·1434 gram H_2O and 0·3685 gram CO_2.

	Theory. $C_{17}H_{32}O_4$.	Found.
C	68·00 per cent.	67·73 per cent.
H	10·66 „	10·74 „
O	21·33 „	21·53 „

The specific gravity of ethyl dipropylpimelate is $d\,4°/4° = 0·9578$; $d\,15°/15° = 0·9495$; $d\,25°/25° = 0·9436$.

The magnetic rotation determinations gave—

t.	Sp. rotation.	Mol. rotation.
18°	0·9834	17·296

The hydrolysis of this ethereal salt was carried out exactly as described under ethyl pimelate. The acid, being sparingly soluble in water, separated as a semi-solid mass on acidifying the solution of the alkaline salt; it was extracted with ether as usual, and thus obtained as a thick oil, which on standing became almost solid. The crystalline cake was very carefully pressed, to remove every trace of oily matter, boiled with a large quantity of water, filtered, and the filtrate allowed to cool slowly. After standing for some time, the milky liquid deposited beautiful, four-sided plates; these were collected, dried, first on a porous plate, then at 50°, and analysed, with the following result:—

0·1400 gram substance gave 0·1258 gram H_2O and 0·3290 gram CO_2.

	Theory. $C_{13}H_{24}O_4$.	Found.
C	63·93 per cent.	64·00 per cent.
H	9·84 „	9·98 „
O	26·23 „	26·02 „

Dipropylpimelic acid is sparingly soluble in hot water, and therefore by the above treatment only small quantities can be recrystallised at a time. It appeared interesting to fractionally crystallise the substance by extracting the residual mass from each crystallisation with fresh quantities of boiling water, until, with the exception of a trace of oily impurity, all had been dissolved. In this way five fractions were obtained, melting respectively at 92—94°, 91—93°, 90—92°, 87—90°, 87—89°; all these fractions on crystallisation from light

petroleum, melted at 95—96°, which must be taken as the correct melting point of the acid, and this behaviour seems to indicate that the crude acid does not consist of two structural isomers.

Dipropylpimelic acid is very sparingly soluble in cold water. 100 parts of water at 13·5° dissolve only 0·049 part of the pure acid.

The dissociation constant for the electrical conductivity of dipropylpimelic acid at different concentrations is K = 0·0030.

Salts of Dipropylpimelic Acid.—The *silver salt*, $C_{13}H_{22}Ag_2O_4$, was prepared by adding silver nitrate to a moderately dilute neutral solution of the potassium salt. It is a white, granular precipitate, apparently insoluble in water. Analysis:—

0·1710 gram substance gave 0·0759 gram H_2O and 0·2142 gram CO_2.

0·3143 gram substance gave, on ignition, 0·1476 gram Ag.

	Theory. $C_{13}H_{22}Ag_2O_4$.	Found.
C	34·13 per cent.	34·33 per cent.
H	4·82 „	4·93 „
Ag.....	47·04 „	46·96 „

A dilute neutral solution of the potassium salt shows the following behaviour with reagents:—

Zinc sulphate, a white, caseous precipitate, insoluble in water. *Lead acetate*, a white, apparently crystalline precipitate, somewhat soluble in boiling water. *Copper sulphate*, a light, bluish-green precipitate, insoluble in water. *Barium* and *calcium chlorides*, no precipitate.

Ethyl Diisopropylpentanetetracarboxylate,

$(COOC_2H_5)_2C(C_3H_7)\cdot[CH_2]_3\cdot C(C_3H_7)(COOC_2H_5)_2$.

The method used and the quantities employed in the preparation of this ethereal salt were the same as in the case of the dipropyl compound, isopropyl iodide being substituted for propyl iodide; the yield of crude product was 42·5 grams.

Ethyl diisopropylpentanetetracarboxylate boils at 250—252° (30 mm.). Analysis:—

0·1648 gram substance gave 0·1335 gram H_2O and 0·3730 gram CO_2.

	Theory. $C_{23}H_{40}O_8$.	Found.
C	62·16 per cent.	61·73 per cent.
H	9·00 „	8·99 „
O	28·83 „	29·28 „

This ethereal salt differs from the normal propyl compound in being a thick syrup, which does not solidify when cooled to 0°. On hydrolysis, it yields a solid acid, presumably the corresponding diisopropylpentanetetracarboxylic acid; it was not analysed.

Ethyl Diisopropylpimelate and Diisopropylpimelic Acid,

$COOH{\cdot}CH(C_3H_7){\cdot}[CH_2]_3{\cdot}CH(C_3H_7){\cdot}COOH.$

In preparing this acid, the acid obtained by the hydrolysis of ethyl diisopropylpentanetetracarboxylate (by the method given on p. 830) was heated at 200° until all effervescence had ceased, and the residual thick, brownish acid converted into the ethyl salt by treatment with alcohol and sulphuric acid. Ethyl diisopropylpimelate, like the normal propyl derivative, must be repeatedly fractioned before it shows a constant boiling point. The specimen used for analysis and for the physical measurements boiled at 220—222° (100 mm.), or only about 4° lower than ethyl dipropylpimelate.

0·1334 gram substance gave 0·1265 gram H_2O and 0·3306 gram CO_2.

	Theory. $C_{17}H_{32}O_4$.	Found.
C	68·00 per cent.	67·58 per cent.
H	10·66 „	10·54 „
O	21·33 „	21·88 „

Ethyl diisopropylpimelate is a thick, colourless oil, boiling at 220—222° (100 mm.). Its specific gravity is $d\ 4°/4° = 0·9651$; $d\ 15°/15° = 0·9567$; $d\ 25°/25° = 0·9507$.

The magnetic rotation determinations gave as an average—

t.	Sp. rotation.	Mol. rotation.
19·3°	0·9866	17·238.

The hydrolysis of this ethereal salt, and the isolation and purification of the resulting acid, were conducted exactly as described under ethyl dipropylpimelate (p. 837). The various fractions obtained by recrystallising the crude acid from water melted at the following temperatures:—93—94°, 92—93°, 91—93°.

These, on recrystallisation from light petroleum, melted at 96—98°, and gave the following numbers on analysis:—

0·1440 gram substance gave 0·1290 gram H_2O and 0·3375 gram CO_2.

	Theory. $C_{12}H_{24}O_4$.	Found.
C	63·93 per cent.	63·92 per cent.
H	9·84 „	9·95 „
O	26·23 „	26·13 „

Diisopropylpimelic acid melts at 96—98°. It is sparingly soluble in cold water; it is, however, about twice as soluble as the isomeric dipropylpimelic acid, 100 parts of water at 13·5° dissolving about 0·096 part of the pure acid. It crystallises from its solution in hot, light petroleum, on cooling, in beautiful, feathery, needle-shaped crystals.

The dissociation constant for the electrical conductivity of diisopropylpimelic acid at different concentrations is $K = 0{\cdot}0032$.

Ethyl Diisobutylpentanetetracarboxylate,

$$(COOC_2H_5)_2C(C_4H_9)\cdot[CH_2]_3\cdot C(C_4H_9)(COOC_2H_5)_2.$$

This ethereal salt could, no doubt, be readily obtained by treating the disodium compound of ethyl pentanetetracarboxylate with isobutyl iodide in the usual way, but it appeared to us interesting to determine whether the synthesis of this substance could equally well be performed by treating the sodium compound of ethyl isobutylmalonate with trimethylene bromide, thus:—

$$2(COOC_2H_5)_2CNa\cdot C_4H_9 + BrCH_2\cdot CH_2\cdot CH_2Br = (COOC_2H_5)_2C(C_4H_9)\cdot CH_2\cdot CH_2\cdot CH_2\cdot C(C_4H_9)(COOC_2H_5)_2 + 2NaBr.$$

138 grams of ethyl isobutylmalonate (b. p. 228—233°) was mixed with a cold solution of 15 grams of sodium dissolved in 170 grams of absolute alcohol, 64·5 grams of trimethylene bromide added, and the mixture heated cautiously on a water-bath, in a flask connected with a reflux apparatus. The reaction sets in all at once, the liquid boils vigorously, and quantities of sodium bromide are deposited. After heating for half an hour, the neutral product was mixed with water, extracted three times with ether, the ethereal solution washed well with water, dried over calcium chloride, and evaporated; the almost colourless, oily residue, which weighed about 150 grams, was then subjected to distillation under reduced pressure (200 mm.). As soon as the last traces of ether had distilled over, the thermometer rose rapidly to 200°, between which temperature and 230° about 80 grams passed over; the pressure was then reduced to 60 mm., when the residue distilled almost completely between 250° and 280°, and weighed 58 grams. The higher fraction was subsequently purified by repeated distillation under a pressure of 30 mm., when a considerable quantity of a colourless oil was obtained boiling constantly at 257—263°. The analysis of this gave the following results:—

0·1354 gram substance gave 0·1134 gram H_2O and 0·3135 gram CO_2.

	Theory. $C_{25}H_{44}O_8$.	Found.
C	63·56 per cent.	63·15 per cent.
H	9·33 „	9·31 „
O	27·11 „	27·54 „

Ethyl diisobutylpentanetetracarboxylate is a very thick, colourless oil which, on long standing, showed signs of crystallising.

Ethyl Diisobutylpimelate and Diisobutylpimelic Acid,

$COOH{\cdot}CH(C_4H_9){\cdot}[CH_2]_3{\cdot}CH(C_4H_9){\cdot}COOH$.

Ethyl diisobutylpentanetetracarboxylate is very readily hydrolysed by boiling with alcoholic potash, but no attempt was made to purify the resulting tetrabasic acid, the crude substance obtained being at once converted into diisobutylpimelic acid.

52 grams of ethyl diisobutylpentanetetracarboxylate (b. p. 250—275°, 30 mm.) was mixed with a solution of 40 grams of pure potassium hydrate dissolved in 90 per cent. methyl alcohol, the mixture boiled in a reflux apparatus for five hours, and evaporated to dryness; the residue was then dissolved in water and boiled until the last traces of methyl alcohol had been expelled. The alkaline solution thus obtained was acidified with hydrochloric acid, and the oily acid which separated extracted four times with pure ether. The ethereal solution was dried over calcium chloride, evaporated, the crude, tetrabasic acid heated at 200—220° until the evolution of carbonic anhydride had entirely ceased, and the residual impure diisobutylpimelic acid converted into the ethyl salt in the usual way.

Ethyl diisobutylpimelate, under a pressure of 100 mm., boils constantly at 235—237°.

The analysis of this substance gave the following results:—

0·1416 gram substance gave 0·1413 gram H_2O and 0·3598 gram CO_2.

	Theory. $C_{19}H_{36}O_4$.	Found.
C.....	69·51 per cent.	69·30 per cent.
H.....	10·98 „	11·09 „
O.....	19·51 „	19·61 „

Ethyl diisobutylpimelate is a colourless oil possessing very similar properties to the other analogously constituted ethereal salts already described.

The specific gravity of this substance is $d\,4°/4° = 0·9444$; $d\,15°/15° = 0·9363$; $d\,25°/25° = 0·9303$.

The magnetic rotation determinations gave as an average—

t.	Sp. rotation.	Mol. rotation.
16·1	0·9952	19·387

The hydrolysis of this ethereal salt was carried out as described under ethyl pimelate. On acidifying the alkaline solution of the potassium salt, the crude diisobutylpimelic acid separates as a thick, gummy mass, and was extracted with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a thick, almost colourless oil which, on standing over sulphuric acid in a vacuum, solidified to a mass of crystals. This crude acid was roughly purified by contact with a porous plate, and then recrystallised from large quantities of boiling water. The analysis gave the following results:—

0·1405 gram substance gave 0·1296 gram H_2O and 0·3399 gram CO_2.

	Theory. $C_{15}H_{28}O_4$.	Found.
C.....	66·17 per cent.	65·98 per cent.
H.....	10·28 „	10·25 „
O.....	23·53 „	23·77 „

Diisobutylpimelic acid melts at about 82—84°, but not very sharply.

It is very sparingly soluble in cold water; 100 parts of water at 13·5° dissolve only about 0·038 part of the pure acid.

The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·1482 gram substance required for neutralisation 0·0605 gram KOH.

A bibasic acid of the formula $C_{15}H_{28}O_4$ requires theoretically 0·0608 gram KOH.

The dissociation constant for the electrical conductivity of diisobutylpimelic acid could not be accurately determined owing to the acid being so sparingly soluble in water.

Ethyl Dibenzylpentanetetracarboxylate,

$(COOC_2H_5)_2C(CH_2{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}C(CH_2{\cdot}C_6H_5)(COOC_2H_5)_2$.

This substance was the first derivative of ethyl pentanetetracarboxylate obtained, and its method of preparation differed essentially from that of the derivatives subsequently investigated, and described in the preceding pages. The quantities taken were:—

Ethyl pentanetetracarboxylate.....	9 grams.
Sodium, dissolved in 15 grams of alcohol	1·2 „
Benzyl chloride.....	9 „

The ethyl pentanetetracarboxylate was dissolved in the cold solution of the sodium ethoxide, the benzyl chloride added, and the mixture heated for two hours in a flask connected with a reflux apparatus.

At the end of this time, the product, which had become quite neutral, was mixed with water, distilled in steam until the excess of benzyl chloride had been completely removed, and the residue extracted with ether. The ethereal solution was dried over anhydrous potassium carbonate, evaporated, and the thick, oily residue allowed to stand over sulphuric acid in a vacuum until it had completely solidified. The crystalline cake was then freed from oily matter by spreading it on a porous plate, rapidly washed with small quantities of methyl alcohol on a filter-pump, and the white, granular residue dried over sulphuric acid in a vacuum. The analysis gave the following result:—

0·1588 gram substance gave 0·1063 gram H_2O and 0·3986 gram CO_2.

	Theory. $C_{31}H_{40}O_8$.	Found.
C.....	68·88 per cent.	68·46 per cent.
H.....	7·41 „	7·43 „
O.....	23·70 „	24·11 „

Ethyl dibenzylpentanetetracarboxylate melts at about 75—77°, and when once melted, it often remains for some days as a very thick, semi-solid, transparent mass, which, however, when rubbed with a rod moistened with methyl alcohol, at once solidifies. It is readily soluble in the usual organic solvents.

Dibenzylpentanetetracarboxylic Acid,

$(COOH)_2C(CH_2{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}C(CH_2{\cdot}C_6H_5)(COOH)_2$.

In order to obtain this acid, the pure ethereal salt (10 grams) was hydrolysed by boiling with excess of methyl alcoholic potash (10 grams KOH) for two hours in a reflux apparatus. The excess of alcohol was distilled off, the product dissolved in water, evaporated on a water-bath till quite free from alcohol, filtered, and acidified with hydrochloric acid. The thick, gummy mass which separated was extracted four times with ether, the ethereal solution well dried over calcium chloride, evaporated, and the thick, oily residue allowed to stand until it had completely solidified. The solid cake thus obtained was roughly purified by spreading it on a porous plate, the crude, yellowish-white acid ground up in a mortar with pure ether, and subsequently washed on a filter-pump with this solvent until the

residual acid was perfectly white. The product consists of pure dibenzylpentanetetracarboxylic acid, as is shown by the following analysis :—

0·1586 gram substance gave 0·0794 gram H_2O and 0·3728 gram CO_2.

	Theory. $C_{23}H_{24}O_8$.	Found.
C.....	64·48 per cent.	64·16 per cent.
H.....	5·61 „	5·55 „
O.....	29·90 „	30·29 „

Dibenzylpentanetetracarboxylic acid decomposes at about 205—207° with evolution of carbonic anhydride and formation of dibenzylpimelic acid :—

$$(COOH)_2(CH_2{\cdot}C_6H_5)C{\cdot}[CH_2]_3{\cdot}C(CH_2{\cdot}C_6H_5)(COOH)_2 = COOH{\cdot}CH(CH_2{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}CH(CH_2{\cdot}C_6H_5){\cdot}COOH + 2CO_2.$$

The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·0972 gram acid required for neutralisation 0·0488 gram KOH.

A tetrabasic acid of the formula $C_{23}H_{24}O_8$ requires 0·0509 gram KOH.

Salts of Dibenzylpentanetetracarboxylic Acid.—The *silver salt*, $C_{23}H_{20}Ag_4O_8$, was prepared from a dilute neutral solution of the ammonium salt by the addition of a large excess of silver nitrate solution, the whole being well shaken during the operation. The white, insoluble precipitate thus obtained, after being well washed with water, and dried over sulphuric acid in a vacuum, gave the following results on analysis :—

0·1667 gram substance gave 0·0406 gram H_2O, 0·1938 gram CO_2, and 0·0842 gram Ag.

	Theory. $C_{23}H_{20}Ag_4O_8$.	Found.
C.....	32·32 per cent.	31·70 per cent.
H.....	2·34 „	2·70 „
Ag.....	50·35 „	50·50 „

A dilute neutral solution of the ammonium salt shows the following behaviour with reagents :—

Copper acetate, a bright-blue precipitate, sparingly soluble in water; on boiling with water, the precipitate becomes almost white. *Calcium chloride*, no precipitate in the cold, but on boiling, the calcium salt

separates as a white, crystalline precipitate. *Barium chloride*, no precipitate. *Zinc sulphate* and *lead acetate*, white, amorphous precipitates insoluble in water.

Dibenzylpimelic Acid,

$$COOH{\cdot}CH(CH_2{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}CH(CH_2{\cdot}C_6H_5){\cdot}COOH.$$

This acid is produced when dibenzylpentanetetracarboxylic acid is heated at 200—220° until the evolution of carbonic anhydride has completely ceased. The resulting brownish resin can only with difficulty be obtained in a crystalline condition; the purification of this crude product may, however, be readily accomplished in the following way:—The crude acid is dissolved in an excess of a warm, dilute solution of barium hydroxide, heated to boiling, and a current of carbonic anhydride passed until the excess of alkali has been removed. The product is filtered, the precipitated barium carbonate well washed, and the colourless filtrate evaporated until a mass of crystals of the barium salt of the acid separates from the boiling solution; these are rapidly collected, washed with a little boiling water on the filter-pump (the salt is more soluble in cold than hot water), and drained on a porous plate. The mother liquors, on continued evaporation, deposit a further crop of crystals, which are collected in the same manner. The colourless, glistening mass of crystals is dissolved in water, acidified with hydrochloric acid, the precipitated acid extracted with ether, and the ethereal solution dried over calcium chloride and evaporated; as the evaporation proceeds, crystals separate; these are collected, freed from a trace of oily impurity by spreading on a porous plate, and then recrystallised from a mixture of equal parts of benzene and light petroleum. In this way, beautiful, glistening, prismatic crystals are obtained which, as the analyses show, consist of pure dibenzylpimelic acid:—

I. 0·1572 gram substance gave 0·1002 gram H_2O and 0·4265 gram CO_2.

II. 0·1355 gram substance gave 0·0888 gram H_2O and 0·3688 gram CO_2.

III. 0·1384 gram substance gave 0·0894 gram H_2O and 0·3758 gram CO_2.

	Theory. $C_{21}H_{24}O_4$.	Found. I.	II.	III.
C	74·12 p. c.	73·99	74·23	74·05 p. c.
H	7·06 „	7·08	7·28	7·17 „
O	18·82 „	18·93	18·49	18·78 „

Dibenzylpimelic acid melts at 120° with slight previous softening; it is readily soluble in hot benzene, ether, and alcohol, sparingly in light petroleum.

The dissociation constant for the electrical conductivity of dibenzylpimelic acid at different concentrations is K = 0·0040.

Salts of Dibenzylpimelic Acid.—The *barium salt*, $C_{21}H_{22}BaO_4 + 3H_2O$(?), is readily prepared by dissolving the pure acid in a solution of barium hydroxide, removing the excess of the latter by passing carbonic anhydride, and evaporating the solution as described above. It is more soluble in cold than in hot water, and separates in pearly plates on boiling its cold concentrated solution.

The analysis of the air-dry salt gave the following results :—

I. 0·5748 gram substance, heated at 100° until constant, lost 0·056 gram H_2O, and the residue, heated with sulphuric acid, gave 0·2554 gram $BaSO_4$.

II. 0·4117 gram substance, heated at 100° till constant, lost 0·0401 gram H_2O.

	Theory.	Found.	
	$C_{21}H_{22}BaO_4 + 3H_2O$.	I.	II.
Ba	25·90 per cent.	26·10	— per cent.
H_2O	10·21 „	9·70	9·74 „

This salt appears to lose some of its water of crystallisation on long standing in the air.

A moderately dilute neutral solution of the potassium salt shows the following behaviour with reagents :—

Barium chloride, on boiling, a white precipitate, sparingly soluble in hot water, but more soluble in cold water. *Calcium chloride*, no precipitate in the cold, but, on boiling, a white calcium salt separates which redissolves on cooling. *Zinc acetate*, a white, caseous precipitate, sparingly soluble in water. *Copper acetate*, a beautiful light-blue precipitate, insoluble in water. *Lead acetate*, a white, amorphous, very sparingly soluble precipitate.

Attempt to Prepare Monobenzylpimelic Acid, $COOH{\cdot}CH(CH_2{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}CH_2{\cdot}COOH$.

In the preceding pages the preparation of some disubstituted derivatives of pimelic acid from the disodium compound of ethyl pentanetetracarboxylate has been described, and it appeared to us of interest to determine whether by employing the monosodium compound of this ethereal salt, monosubstituted derivatives such as monomethyl- and monobenzyl-pimelic acids would also be obtained. The example selected was the preparation of monobenzylpimelic acid,

as it was thought probable that the reaction could be more readily followed in this case than in the case of the lower homologues.

9 grams of ethyl pentanetetracarboxylate (1 mol.) was mixed with a solution of 0·6 gram of sodium (1 mol.) in absolute alcohol, 4 grams of benzyl chloride (1 mol.) added, and the mixture heated in a reflux apparatus for two hours. The product was then diluted with water, extracted with ether, and the ethereal solution washed well, dried over calcium chloride, and evaporated. In this way, 11 grams of a yellowish oil was obtained, which, even on long standing over sulphuric acid in a vacuum, did not crystallise, although a distinct scum formed on the surface.

The ethereal salt was hydrolysed by boiling with a methyl alcoholic solution of 11 grams of potassium hydrate for two hours, the alcohol removed by evaporation with the addition of water, and the cold alkaline solution acidified with dilute hydrochloric acid. The thick, resinous mass which separated was extracted ten times with ether, the ethereal solution dried over calcium chloride, evaporated, and the transparent, resinous mass, which, even after standing for some days over sulphuric acid in a vacuum, showed no signs of crystallising, was stirred well with warm water of 40°. In a short time the mass began to get hard and opaque, and on constantly changing the water a solid mass was ultimately obtained. This was dried on a porous plate at the ordinary temperature, ground up in a mortar with pure ether, and the insoluble tetracarboxylic acid which separates washed on a filter pump with small quantities of ether until it had become perfectly colourless.

The analysis of the substance, dried over sulphuric acid in a vacuum, gave:—

0·1376 gram substance gave 0·0744 gram H_2O and 0·3239 gram H_2O.

	Theory.		
	Monobenzylpentane-tetracarboxylic acid $= C_{16}H_{18}O_8$.	Dibenzylpentane-tetracarboxylic acid $= C_{23}H_{24}O_8$.	Found.
C	56·80 p. c.	64·48 p. c.	64·20 p. c.
H.....	5·33 „	5·61 „	6·01 „
O.....	37·87 „	29·90 „	29·79 „

Dibenzylpentanetetracarboxylic acid had therefore been formed in this reaction instead of the monobenzyl derivative. This interesting point was confirmed by an investigation of the properties of the acid, and an analysis of the silver salt:—

0·2120 gram of the dry silver salt gave on ignition 0·1063 gram Ag.

	Theory. $C_{23}H_{20}Ag_4O_8$.	Found.
Ag.....	50·35 per cent.	50·14 per cent.

In order, if possible, to further follow the course of this reaction, the aqueous extract of the crude dibenzylpentanetetracarboxylic acid (see above) was carefully examined. The combined extracts were neutralised with sodium hydrate, evaporated to a small bulk, acidified, extracted with pure ether, the ethereal solution dried over calcium chloride and evaporated, and the residual, thick, yellow oil allowed to stand for some days over sulphuric acid in a vacuum. As the oil showed no signs of crystallising, it was transferred to a flask, and heated in an oil-bath at 220° until the evolution of carbonic anhydride had ceased. The residual, dark-coloured acid was then dissolved in dilute sodium hydrate solution, boiled for two hours with freshly-ignited animal charcoal, and filtered. The almost colourless alkaline solution was evaporated to a small bulk, acidified, extracted five times with ether, the ethereal solution dried over calcium chloride, evaporated, and the oily residue set aside until it had completely solidified. The crude product, which showed the properties of pimelic acid, was roughly purified by spreading it on a porous plate, then converted into the calcium salt, and this salt, after recrystallisation, decomposed with hydrochloric acid, and the resulting acid finally recrystallised from benzene.

The white, crystalline powder thus obtained melted at 100—102° and consisted of pure pimelic acid, as is shown by the following analysis:—

0·1322 gram substance gave 0·0908 gram H_2O and 0·2542 gram CO_2.

	Theory. $COOH\cdot[CH_2]_5\cdot COOH$.	Found.
C	52·50 per cent.	52·44 per cent.
H	7·50 „	7·63 „
O	40·00 „	39·93 „

This experiment proves that, under the conditions employed, ethyl monobenzylpentanetetracarboxylate is not formed, the reaction, on the contrary, giving rise to the production of ethyl dibenzylpentanetetracarboxylate; one half of the ethyl pentanetetracarboxylate either takes no part whatever in the decomposition or is regenerated from the monosodium compound, as shown in the introduction.

Action of Benzal Chloride on the Disodium Compound of Ethyl Pentanetetracarboxylate. Formation of Dibenzalpimelic Acid,

$$COOH{\cdot}C(:CH{\cdot}C_6H_5){\cdot}[CH_2]_3{\cdot}C(:CH{\cdot}C_6H_5){\cdot}COOH.$$

This remarkable reaction was first instituted with the object of preparing phenylhexamethylene derivatives, as explained in the introduction. 9 grams of ethyl pentanetetracarboxylate was dissolved in a solution of 1·2 grams of sodium in 30 grams of absolute alcohol, 4·2 grams of benzal chloride added, and the mixture heated for five hours in a flask connected with a reflux apparatus. The product was then mixed with water, extracted with ether, the ethereal solution washed with water, and evaporated, and the residual thick, yellowish oil hydrolysed by boiling it with twice the calculated quantity of methyl alcoholic potash for three hours. The alcohol was removed by mixing the product with water and boiling vigorously, the cold alkaline solution acidified with hydrochloric acid, and the resinous precipitate extracted with ether. The ethereal solution was then evaporated, and the yellow, oily residue stirred for two days with fresh quantities of water, until it had become quite solid.

The very crude acid thus obtained was collected, washed with water, allowed to dry on a porous plate, and then heated at 200—220°, until the evolution of carbonic anhydride had ceased. The dark-brown residue was dissolved in dilute sodium hydrate, and the solution boiled with freshly-ignited animal charcoal, by which means a quantity of impurity was removed; the acid was then reprecipitated with hydrochloric acid, washed well, and allowed to dry on a porous plate. The thoroughly dry, dark-yellow substance was ground up in a mortar, exhausted three times with boiling benzene, the residue dissolved in methyl alcohol, and the solution allowed to evaporate nearly to dryness at the ordinary temperature.

The crystals which were deposited were collected, washed with methyl alcohol, recrystallised twice from this solvent, and the magnificent, glistening prisms thus obtained analysed, with the following result:—

I. 0·1192 gram substance gave 0·0672 gram H_2O and 0·3270 gram CO_2.

II. 0·1521 gram substance gave 0·0834 gram H_2O and 0·4183 gram CO_2.

	Theory. $C_{21}H_{20}O_4$.	Found. I.	Found. II.
C	75·00 per cent.	74·81	75·00 per cent.
H	5·95 ,,	6·26	6·09 ,,
O	19·05 ,,	18·93	18·91 ,,

Dibenzalpimelic acid melts at 192—193°. It is readily soluble in hot ethyl and methyl alcohol, sparingly in chloroform and carbon bisulphide, and only very sparingly in benzene, toluene, light petroleum, and water. When strongly heated in small quantities in a test-tube, the acid distils with apparently very little decomposition, and the slightly yellowish distillate solidifies completely on rubbing with a glass rod. Dibenzalpimelic acid, being an unsaturated acid, is instantly oxidised by potassium permanganate in alkaline solution, and at the same time a very strong odour of benzaldehyde is noticeable.

The basicity of the acid was determined first by titration with a standard solution of potassium hydrate:—

0·1264 gram of the pure acid required for neutralisation 0·0425 gram KOH.

This amount of a bibasic acid of the formula $C_{21}H_{20}O_4$ requires 0·0421 gram KOH.

Salts of Dibenzalpimelic Acid.—The *silver salt*, $C_{21}H_{18}O_4Ag_2$, was prepared by adding silver nitrate to a neutral solution of the potassium salt. The white, amorphous precipitate thus produced was collected, washed with water, dried over sulphuric acid on a porous plate, and analysed, with the following result:—

0·1990 gram substance gave 0·0586 gram H_2O and 0·3314 gram CO_2.

0·3108 gram substance gave on ignition 0·1232 gram Ag.

	Theory. $C_{21}H_{18}O_4Ag_2$.	Found.
C	45·90 per cent.	45·42 per cent.
H	3·28 „	3·27 „
Ag.....	39·16 „	39·63 „

The neutral solution of the potassium salt gives, with solutions of *barium chloride*, *calcium chloride*, *zinc sulphate*, and *lead acetate*, white, amorphous precipitates, almost insoluble in water. *Copper sulphate* gives a fine, pale-blue, amorphous precipitate, almost insoluble in water.

In order, if possible, to obtain some further clue to the formation of dibenzalpimelic acid in the above decomposition, the aqueous liquors from the hydrolysis of the crude product of the reaction, from which the crude dibenzalpimelic acid had been precipitated by hydrochloric acid, as described above, were extracted five times with ether, the ethereal extract carefully dried over calcium chloride and evaporated. A small quantity of an oily acid was thus obtained, which, after purification by conversion into the calcium salt and recrystallisation

from benzene, melted at 100—102°, and showed all the properties of pimelic acid. There could be no doubt as to its identity, although the quantity was too small for analysis.

It appears, therefore, that in this decomposition some ethyl pentanetetracarboxylate is regenerated, which, on hydrolysis and subsequent heating at 200°, is converted into pimelic acid.

For convenience of reference we append, in tabular form, the principal properties of the substances described in this paper.

Pentanetetracarboxylic Acid and its Derivatives.

	Decomposing point.	Boiling point of ethyl salt (30 mm.).
Pentanetetracarboxylic acid	Above 120°	230—235°
Dimethylpentanetetracarboxylic acid.....	200—205°	238—240°
Diethylpentanetetracarboxylic acid	192—195°	247°
Dipropylpentanetetracarboxylic acid	—	253—256° (M. p. =52—54°)
Diisopropylpentanetetracarboxylic acid.....	—	250—252°
Diisobutylpentanetetracarboxylic acid.....	—	257—263°
Dibenzylpentanetetracarboxylic acid.....	205—207°	(M. p. = 75—77°)
Dibromopentanetetracarboxylic acid	—	(M. p. = 45°).

Pimelic Acid and its Derivatives.

	Acid.			Ethyl salt.		
	Melting point.	Solubility in 100 pts. of water at 13·5°.	Dissociation constants = K.	Boiling point (100 mm.).	Sp. gr. at 15°/15°.	Magnetic rotation.
Pimelic acid.....	100—102°	2·52	0·00341	192—194°	0·9988	11·424
Dimethylpimelic acid	74—76	2·19	0·00337	195—196	0·9728	13·298
Diethylpimelic acid	96—97	0·234	0·00345	209—210	0·9583	15·355
Dipropylpimelic acid	95—96	0·049	0·0030	224—226	0·9495	17·296
Diisopropylpimelic acid	96—98	0·096	0·0032	220—222	0·9567	17·238
Diisobutylpimelic acid	82—84	0·038	—	235—237	0·9363	19·387
Dibenzylpimelic acid	120	—	0·0040	—	—	—
Dibenzalpimelic acid	192—193	—	—	—	—	—

LONDON:
HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Action of Methylene Iodide on the Disodium Compound of Ethyl Pentanetetracarboxylate. Synthesis of Hexamethylene Derivatives.

By W. H. Perkin, Jun., Ph.D., F.R.S.

When trimethylene bromide is treated with the mono-sodium compound of ethyl malonate, the reaction proceeds in two distinct phases (Trans., 1887, **51**, 1, 241). In the first place, ethyl tetramethylenedicarboxylate is formed with regeneration of a corresponding amount of ethyl malonate, thus :—

$$2CHNa(COOC_2H_5)_2 + CH_2Br{\cdot}CH_2{\cdot}CH_2Br =$$
$$CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}>C(COOC_2H_5)_2 + CH_2(COOC_2H_5)_2 + 2NaBr,$$

whilst the second reaction consists in the production of ethyl pentanetetracarboxylate, thus :—

$$2CHNa(COOC_2H_5)_2 + CH_2Br{\cdot}CH_2{\cdot}CH_2Br =$$
$$(COOC_2H_5)_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(COOC_2H_5)_2 + 2NaBr.$$

This ethereal salt has been found to be of very great service in synthetical experiments, owing to the fact that when treated with sodium ethylate, it yields a disodium compound,

$$(COOC_2H_5)_2CNa{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CNa(COOC_2H_5)_2,$$

which reacts readily with alkyl haloïds yielding, indirectly, derivatives of pimelic acid (see the next paper), and which has also been employed in the synthesis of pentamethylene derivatives (Trans., 1887, **51**, 241).

In the course of these experiments it seemed probable that very interesting results might be obtained by the study of the action of methylene iodide, ethylene bromide, trimethylene bromide, and other similar alkylene haloïds on this disodium compound, and I beg now to lay before the Society a short account of the results which have been obtained in the case of methylene iodide, reserving for a future paper the consideration of the action of the other alkylene haloïds on this disodium compound.

At 100°, methylene iodide reacts readily with an alcoholic solution of the disodium compound of ethyl pentanetetracarboxylate with separation of sodium iodide and formation of ethyl hexamethylenetetracarboxylate, thus :—

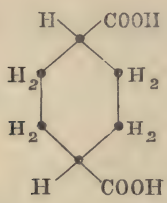
$$H_2C<\begin{matrix}CH_2{\cdot}CNa(COOC_2H_5)_2\\CH_2{\cdot}CNa(COOC_2H_5)_2\end{matrix} + CH_2I_2 = H_2C<\begin{matrix}CH_2{\cdot}C(COOC_2H_5)_2\\>CH_2\\CH_2{\cdot}C(COOC_2H_5)_2\end{matrix} + 2NaI.$$

This ethereal salt, on hydrolysis, yields the corresponding hexamethylenetetracarboxylic acid, and this beautifully crystalline substance, when heated at 200—220°, is decomposed with evolution of 2 mols. of CO_2 and formation of *two isomeric* hexamethylenemetadicarboxylic or *hexahydroisophthalic acids :*

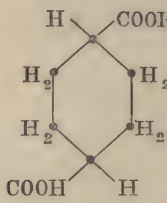
$$H_2C\begin{<}{CH_2\cdot C(COOH)_2}{>CH_2}{CH_2\cdot C(COOH)_2} = H_2C\begin{<}{CH_2\cdot CH\cdot COOH}{>CH_2}{CH_2\cdot CH\cdot COOH} + 2CO_2.$$

In order to understand this interesting decomposition, it will be well to compare these compounds with the corresponding hexahydroterephthalic acids, which have been so carefully investigated by Baeyer.

Baeyer, in his classical researches on the reduction of terephthalic acid (*Annalen*, **245**, 103; **251**, 257), has shown that hexahydroterephthalic acid, which contains two *relatively* asymmetrical carbon atoms (*Annalen*, **245**, 130), is capable of existing in two modifications; these he formulates and designates thus :—*



Maleïnoïd (or Γ^{cis}) hexahydroterephthalic acid.



Fumaroïd (or $\Gamma^{cistrans}$) hexahydroterephthalic acid.

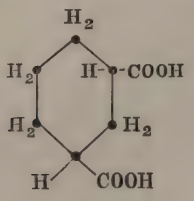
The Γ^{cis} or maleïnoïd form is the labile modification, as it is converted into the $\Gamma^{cistrans}$ or fumaroïd form by heating with concentrated hydrochloric acid at 180°. The former is readily soluble in water, melts at 160°, and crystallises in large crystals like maleïc acid; the latter is sparingly soluble in water, sublimes on heating, and crystallises in short prisms, like fumaric acid.

Similarly, hexahydrophthalic acid, trimethylenedicarboxylic acid [1 : 2], the symmetrical substitution derivatives of succinic acid, and other analogously constituted acids have been found to exist in structurally isomeric forms, and in each case the evidence has been in favour of the assumption that the higher melting and less soluble isomeride is the $\Gamma^{cistrans}$ or fumaroïd modification.

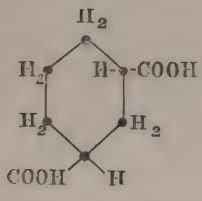
An examination of the formula of hexamethylenemetadicarboxylic acid shows at once that this acid also contains two *relatively* asym-

* The dots represent carbon atoms as in Baeyer's paper.

metrical carbon atoms, and this fact would lead to the supposition that this acid must also occur in two modifications, thus :—



Maleïnoïd (or Γ^{cis}) hexamethylenemetadicarboxylic acid.

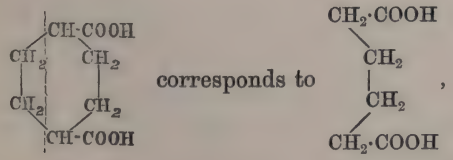


Fumaroïd (or Γ^{cistrans}) hexamethylenemetadicarboxylic acid.

The investigation of the substance obtained from hexamethylenetetracarboxylic acid by the elimination of 2 mols. of CO_2 has shown that this product is, as theory indicates, a mixture of two isomeric acids, which may be separated by repeated recrystallisation, or better, by means of their calcium salts.

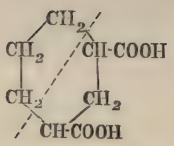
Of these two acids, the more soluble isomeride, which melts at 118—120°, was at first thought to be the Γ^{cis} or maleïnoïd acid, in which case the less soluble acid, which melts at 161—163°, would be the corresponding Γ^{cistrans} or fumaroïd modification. On carefully examining the properties of these two acids, results were obtained which, as it appears to me, prove that the reverse is the case, and that the acid which has the higher melting point and lesser solubility must be represented as the maleïnoïd form.

Baeyer, in the course of his experiments on the constitution of benzene, was led to the conclusion that the reduction products of terephthalic acid no longer behave as benzene derivatives; they show, on the contrary, the properties of saturated and unsaturated compounds of the fatty series, even in the minutest details (*Annalen*, **251**, 257); thus hexahydroterephthalic acid may be compared with adipic acid:

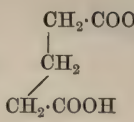


and as adipic acid gives no anhydride, so also no anhydride could be obtained from Γ^{cis} hexahydroterephthalic acid (*Annalen*, **245**, 174).

Hexamethylenemetadicarboxylic acid may, on the other hand, be compared with glutaric acid:



corresponds to



,

but glutaric acid, as Markownikow has shown (*Jour. Russ. Chem. Soc.*, **9**, 283), readily yields an anhydride when heated with acetyl chloride; it therefore follows, if the analogy between the two acids holds good, that hexamethylenemetadicarboxylic acid should also give an anhydride.

On subjecting this hypothesis to the test of experiment, it was found that not only does the acid of lower melting point give an anhydride, but that both the isomeric hexamethylenemetadicarboxylic acids, when treated with acetyl chloride, yield with great ease *the same* anhydride, and this anhydride, when dissolved in water, is converted quantitatively into the acid melting at 161—163°, which must therefore be the Γ^{cis} or maleïnoïd acid. By conversion into the anhydride, and subsequent decomposition of this substance by water, it is thus possible to convert the $\Gamma^{cistrans}$ acid (m. p. 118—120°) quantitatively into the isomeric Γ^{cis} acid (m. p. 161—163°).

In discussing the nature of the hexahydroterephthalic and hexahydrophthalic acids, both of which exist in isomeric forms, Baeyer lays great stress not only on the anhydride formation, but also on the behaviour of the acids when heated with hydrochloric acid at 180°, as a means of distinguishing the Γ^{cis} and $\Gamma^{cistrans}$ modifications. In both cases under these circumstances, the lower melting or more soluble isomeride is converted into the higher melting and less soluble modification; the former Baeyer represents as the Γ^{cis} or maleïnoïd acid, the latter as the $\Gamma^{cistrans}$ or fumaroïd acid.

With a view to obtaining further evidence as to the nature of the two isomeric hexamethylenemetadicarboxylic acids, it was therefore important that the action of hydrochloric acid on the two acids should be carefully investigated. The results obtained in this investigation were very remarkable; the $\Gamma^{ristrans}$ acid of low melting point is converted by this treatment in part into the Γ^{cis} acid of high melting point, and the acid of high melting point is similarly, in part, converted into the acid of low melting point, but in both cases a considerable quantity of the original acid remains unchanged, and it would seem probable that the conversion of each modification into the other goes on until a certain equilibrium has been established, and then hydrochloric acid has no further action.

The only direct evidence at present obtained which throws any light on the constitution of these two hexamethylenedicarboxylic acids is,

therefore, the fact that the anhydride, which is apparently equally readily obtained from each, and which must be the anhydride of the maleïnoïd acid, when dissolved in water, yields the acid melting at 161—163°, just as maleïc anhydride, when dissolved in water, yields maleïc acid.

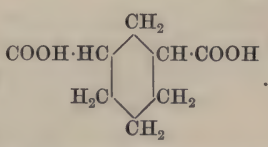
Therefore, as no evidence to the contrary has as yet been obtained, the acid melting at 161—163° is assumed to be Γ^{cis} hexamethylenemetadicarboxylic acid, and the acid melting at 118—120° is represented as $\Gamma^{cistrans}$ hexamethylenemetadicarboxylic acid.

So far it has been assumed that these acids are derivatives of hexamethylene, and there can be no doubt that this is the case, from the following considerations:—

1. Potassium permanganate is without action on dilute sodium carbonate solutions of these acids at the ordinary temperature, and, therefore, these acids cannot be unsaturated compounds (Baeyer, *Annalen*, **245**, 146).

2. These acids are capable of yielding anhydrides. This is only possible when the carboxyl groups in the original pimelic acid are approximated: and this can only be brought about by the formation of a ring in such a way that the carboxyl groups, which were originally separated by five carbon atoms, are now, by insertion of a methylene group and formation of a ring, only separated by three carbon atoms, as in glutaric acid:

$COOH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH$ becomes

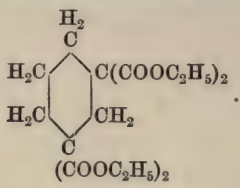


Further experiments on these interesting acids are in progress, and it is proposed to include also a study of pentamethylenedicarboxylic acid, $CH_2<\begin{matrix}CH_2{\cdot}CH{\cdot}COOH\\ CH_2{\cdot}CH{\cdot}COOH\end{matrix}$, and tetrahydronaphthalenedicarboxylic acid, $C_6H_4<\begin{matrix}CH_2{\cdot}CH{\cdot}COOH\\ CH_2{\cdot}CH{\cdot}COOH\end{matrix}$, with a view to determining whether these two substances are also capable of existing in structurally isomeric modifications.

It is unfortunate that, owing to the formation of bye-products of complicated constitution, the yield of the hexamethylenedicarboxylic acids obtained by the method described in this paper is so small; but it is hoped that, by varying the conditions employed, this yield may be ultimately improved.

In conclusion, I must express my thanks to Mr. Bertram Prentice for his very valuable help in carrying out this investigation.

Ethyl Hexamethylenetetracarboxylate [1 : 1 : 3 : 3],



In preparing this ethereal salt, the following quantities were used in each operation :—

Ethyl pentanetetracarboxylate.....	36·0 grams.
Sodium (dissolved in 50 grams of alcohol)	4·6 „
Methylene iodide	28·0 „

The ethyl pentanetetracarboxylate was mixed with the cold solution of the sodium ethylate in a soda-water bottle, the methylene iodide then added, the bottle securely corked and tied down, and warmed in a water-bath to about 50° with frequent agitation, until the layer of methylene iodide, which separates out on the bottom of the bottle, has completely dissolved. The water was then slowly raised to the boiling point, and the bottle kept at this temperature for six hours.

The product was then mixed with water, extracted three times with ether, the ethereal solution washed with water containing a little sulphurous acid (to remove traces of iodine), dried over calcium chloride, evaporated, and the resulting oil, which weighs about 34 grams, purified by fractionation under reduced pressure (50 mm.). A considerable quantity of a thick oil was thus obtained, which boiled at 235—255° (50 mm.), but there was a large, dark-coloured residue in the retort, which could not be distilled without decomposition. On refractioning the distillate, the product was ultimately obtained pure, as a colourless oil, boiling constantly at 243—245° under a pressure of 50 mm. This preparation gave the following numbers on analysis :—

I. 0·1662 gram substance gave 0·1188 gram H_2O and 0·3538 gram CO_2.

II. 0·1723 gram substance gave 0·1195 gram H_2O and 0·3680 gram CO_2.

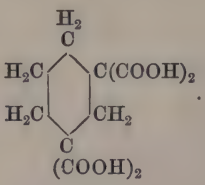
	Theory. $C_{18}H_{28}O_8$.	Found. I.	Found. II.
C	58·06 per cent.	58·33	58·25 per cent.
H	7·53 „	7·94	7·70 „
O	34·40 „	33·73	34·05 „

The molecular weight of this ethereal salt was determined by Raoult's method with the following result, using acetic acid as the solvent:—

Weight of substance taken	1·1417 grams.
Weight of acetic acid	45·37 „
Melting point of the acetic acid	15·959°
Melting point of the mixture	15·685°
Depression of the melting point	0·274°
Molecular weight calculated from these data	= 359
Theory for $C_{15}H_{28}O_8$	= 372

Ethyl hexamethylenetetracarboxylate is a thick, colourless oil, resembling ethyl pentanetetracarboxylate in its general properties. It is readily hydrolysed by boiling with alcoholic potash, with formation of the potassium salt of hexamethylenetetracarboxylic acid [1 : 1 : 3 : 3].

Hexamethylenetetracarboxylic Acid [1 : 1 : 3 : 3],



The purification of the crude product of the action of methylene iodide on the sodium compound of ethyl pentanetetracarboxylate, by fractionation, is always attended with great loss, as the oils of high boiling point contained in this crude product retard the distillation of the ethyl hexamethylenetetracarboxylate, and if the temperature is raised sufficiently high to distil over all the ethereal salt, rapid decomposition sets in. It is possible, however, to avoid this distillation, as considerable quantities of hexamethylenetetracarboxylic acid may be prepared directly from the crude ethereal salt in the following way:—

The crude ethereal salt (1 mol.) is gradually added to a methyl alcoholic solution of pure potassium hydrate (6 mols.), contained in a flask, and the mixture, as soon as the somewhat violent reaction has subsided, heated to boiling in a reflux apparatus on a water-bath for four hours. The alcohol is then distilled off, the residue dissolved in water, and evaporated on a water-bath till quite free from alcohol, the cold aqueous solution acidified with hydrochloric acid, all rise of temperature being avoided by cooling with water, and the product extracted at least 20 times with ether.

A curious phenomenon is noticeable during this operation; the liquid separates into three layers; the upper layer is the ethereal

extract, the lower one the aqueous solution of the salts, and the middle layer is a thick, brownish-coloured oil, which, on shaking with ether, dissolves only to a small extent. This syrupy substance has only been superficially examined; it consists apparently of an acid of very complicated constitution, which evidently can be purified only with great difficulty.

The ethereal extract is dried over calcium chloride, evaporated to a small bulk, and allowed to stand in a cool place for a week, at the end of which time a thick, crystalline crust forms on the bottom of the flask. This is freed, as far as possible, from the ethereal solution of the oily impurities, by filtration on a pump, the residue washed with small quantities of pure ether until perfectly colourless, and then spread on a porous plate. The white, crystalline mass thus obtained, which is almost pure hexamethylenetetracarboxylic acid, is cautiously warmed with water to about 80° until completely dissolved, and the solution filtered, and allowed to stand in a cool place for five or six days. The acid gradually separates in magnificent, colourless, glistening prisms; these are collected, washed with water, and dried on a porous plate over sulphuric acid in a vacuum. When analysed they gave the following results:—

I. 0·1661 gram substance gave 0·0720 gram H_2O and 0·2810 gram CO_2.

II. 0·1776 gram substance gave 0·0774 gram H_2O and 0·3016 gram CO_2.

III. 0·1554 gram substance gave 0·0699 gram H_2O and 0·2666 gram CO_2.

	Theory. $C_{10}H_{12}O_8$.	Found. I.	II.	III.
C	46·15 p. c.	46·14	46·31	46·78 p. c.
H	4·61 „	4·81	4·84	4·98 „
O	49·23 „	49·05	48·85	48·24 „

Analysis III was made with a sample of the acid, before recrystallisation from water.

Hexamethylenetetracarboxylic acid is readily soluble in hot, and moderately in cold, water; it dissolves freely in hot alcohol, but is only very sparingly soluble in ether. When heated rapidly in a capillary tube, it decomposes at about 218—220° with evolution of carbonic anhydride and formation of a mixture of Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenedicarboxylic acids, as explained in the introduction.

The basicity of this acid was determined, in the first place, by titration with standard potassium hydrate solution.

1·2001 grams of the pure acid required for neutralisation 184·5 c.c.

of potassium hydrate solution (1 c.c. = 0·00559 gram KOH = 1·0313 grams KOH).

A tetrabasic acid of the formula $C_{10}H_{12}O_8$ requires for neutralisation 1·0302 gram KOH.

The *silver salt* of *hexamethylenetetracarboxylic acid*, $Ag_4C_{10}H_8O_8$, was prepared by adding a large excess of a strong solution of silver nitrate to the neutral solution of the potassium salt, prepared as above. The voluminous, white, gelatinous precipitate thus obtained was collected, washed well on a filter pump, dried first over sulphuric acid in a vacuum, then at 100°, and analysed, with the following result:—

0·3460 gram substance gave 0·0430 gram H_2O and 0·2168 gram CO_2.

0·2614 gram substance left, after ignition, 0·1630 gram Ag.

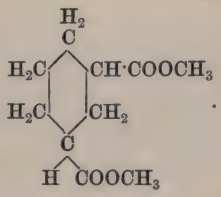
	Theory. $C_{10}H_8O_8Ag_4$.	Found.
C	17·48 per cent.	17·09 per cent.
H.....	1·17 „	1·37 „
Ag.....	62·70 „	62·32 „

The silver salt is very stable and only very slowly darkened when exposed to diffused light; it is also very sparingly soluble in water.

A dilute solution of the potassium salt of hexamethylenetetracarboxylic acid shows the following behaviour with reagents:—

Barium chloride, no precipitate in the cold, but, on heating, a white, apparently crystalline salt separates, which redissolves on cooling. *Calcium chloride* shows a similar behaviour. *Copper sulphate*, no precipitate in the cold, but, on boiling, the solution becomes intensely blue and deposits a small quantity of a light-blue precipitate. *Copper acetate* gives, in the cold, a pale-blue precipitate, which is much increased by boiling. *Lead acetate*, a white, gelatinous precipitate, sparingly soluble in water.

Methyl Hexamethylenemetadicarboxylate,



Hexamethylenetetracarboxylic acid, when heated at 200—220°, is, as has already been stated, decomposed with evolution of 2 mols. CO_2 and formation of two isomeric hexamethylenemetadicarboxylic acids.

The amount of the tetracarboxylic acid obtained as described above is small, and although the dark-coloured ethereal mother liquors still

contain considerable quantities of this acid, no method could be devised by which it could readily be extracted. Fortunately, the hexamethylenedicarboxylic acids can be obtained from this crude product without further purification, the following method, which has been repeatedly employed, giving satisfactory results.

The crude, dark-brown acid which is left behind after distilling the ether from the mother liquors of the pure hexamethylenetetracarboxylic acid, and which weighed about 122 grams, was heated at 220—230° until the evolution of carbonic anhydride had ceased; the residue (73 grams) was dissolved in 4—6 times its weight of methyl alcohol, mixed with about 50 grams of concentrated sulphuric acid, and the mixture heated to boiling on a reflux apparatus for 5 hours. The product was then poured into a large volume of water, extracted four times with ether, the ethereal solution washed twice with very dilute sodium carbonate solution, dried over anhydrous potassium carbonate, evaporated, and the residual dark-brown oil (71 grams) purified by rapid fractionation under reduced pressure (60 mm.). About 28 grams distilled between 170° and 177° as a colourless oil, leaving a quantity of a dark-coloured residue of very high boiling point in the retort. On repeated fractionation, the methyl salt was obtained pure, boiling at 172—175° (60 mm.); the analysis gave the following results:—

0·1626 gram substance gave 0·1192 gram H_2O and 0·3578 gram CO_2.

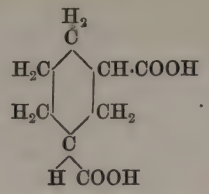
	Theory. $C_{10}H_{16}O_4$.	Found.
C	60·00 per cent.	60·00 per cent.
H	8·00 „	8·14 „
O	32·00 „	31·86 „

The molecular weight of this ethereal salt was determined by Raoult's method, with the following result, using acetic acid as the solvent:—

Weight of substance taken	1·0117 gram.
Weight of acetic acid taken.....	50·21 „
Depression of the melting point	0·373°
Molecular weight calculated from these data	= 211
Theory for $C_{10}H_{16}O_4$	= 200

This ethereal salt is a mixture of the methyl salts of Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenedicarboxylic acid. It is a colourless, fairly mobile liquid, which possesses an odour closely resembling that of the ethereal salts of the higher members of the succinic series.

[1]^{cis} *Hexamethylenemetadicarboxylic Acid,*



The hydrolysis of methyl hexamethylenedicarboxylate is readily carried out by boiling the pure methyl salt with $1\frac{1}{2}$ times the calculated quantity of alcoholic potash for two hours on a water-bath. The product is evaporated nearly to dryness, the residue dissolved in water, vigorously boiled until the last traces of alcohol have been expelled, and the cold alkaline solution acidified with hydrochloric acid and extracted five times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating, deposits a thick, almost colourless oil, which, on standing over sulphuric acid in a vacuum, gradually solidifies, and in about 14 days is converted into a hard cake of crystals. The crude acid thus obtained is spread on a porous plate, allowed to stand until all traces of oily impurity have been absorbed, the resulting colourless mass dissolved in boiling benzene, mixed with light petroleum (b. p. 60—70°) until a slight turbidity is noticeable, the solution again heated to boiling, and then allowed to stand in a cool place for two or three days. In this way a quantity of a hard, white, crystalline substance was obtained, which was collected, washed with cold benzene, dried on a porous plate at 80°, and analysed with the following result:—

0·1442 gram substance gave 0·0930 gram H_2O and 0·2954 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found.
C	55·81 per cent.	55·88 per cent.
H	6·98 „	7·16 „
O	37·21 „	36·96 „

This analysis agrees well with the formula of hexamethylenedicarboxylic acid, and the general behaviour of the acid, and especially the stability of its sodium salt to potassium permanganate, is in accordance with this view, but the substance is, nevertheless, not a definite compound, as the following experiment shows.

When heated in a capillary tube, the acid shows no definite melting point; the crystals begin to soften at 116°, and are not completely melted when the temperature has risen to 135°. The reason for this behaviour was found, on further investigation, to be due to the fact that the substance is a mixture of varying proportions of two isomeric acids,

$C_8H_{12}O_4$, that is, of Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenemetadicarboxylic acids. At first the separation of these two isomerides was accomplished by oft-repeated recrystallisation, first from benzene, then from a mixture of benzene and light petroleum, and finally from concentrated hydrochloric acid; the less soluble (Γ^{cis}) acid was found to melt at 159—161°, the more readily soluble ($\Gamma^{cistrans}$) acid at 118—120°.

Subsequently, it was discovered that the separation could be much more readily effected by taking advantage of the fact that the calcium salt of Γ^{cis} hexamethylenedicarboxylic acid is much less soluble in water than that of the $\Gamma^{cistrans}$ dicarboxylic acid. The mixed acids, after one crystallisation from benzene and light petroleum, are dissolved in a considerable bulk of water, the solution heated to about 50° and agitated with a very slight excess of calcium carbonate, care being taken that enough water is present to prevent the precipitation of the sparingly soluble calcium salt of the Γ^{cis} acid. The solution is then filtered from the slight excess of calcium carbonate, and evaporated on a water-bath until a considerable crop of crystals has formed; these are collected, washed well with hot water, and the evaporation of the filtrate and subsequent separation of the crystals formed continued until only a small bulk of liquid remains.

The various crops of crystals consist of the almost pure calcium salt of Γ^{cis} hexamethylenedicarboxylic acid, the very soluble calcium salt of the isomeric acid remaining in solution.

In order to obtain the free Γ^{cis} acid, the crystals are boiled with sufficient concentrated hydrochloric acid to dissolve them, and the solution filtered through glass wool and set aside to cool slowly. The mass of needle-shaped crystals thus obtained, after washing with concentrated hydrochloric acid, recrystallising from this solvent, and drying at 100°, melted not quite sharply at 159—162°; the substance was, therefore, again converted into the calcium salt, the regenerated acid twice recrystallised from concentrated hydrochloric acid, and the beautiful, colourless crystals, which melted at 161—163°, analysed with the following result:—

I. 0·1370 gram substance gave 0·0882 gram H_2O and 0·2806 gram CO_2.

II. 0·1507 gram substance gave 0·0969 gram H_2O and 0·3081 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found. I.	Found. II.
C	55·81 per cent.	55·86	55·75 per cent.
H	6·98 „	7·15	7·14 „
O	37·21 „	36·99	37·11 „

Γ^{cis} *Hexamethylenedicarboxylic acid* melts at 161—163°. It is very

soluble in warm water, benzene, and alcohol, and moderately so in ether, but only sparingly in light petroleum; it crystallises well from water or benzene, but best from boiling concentrated hydrochloric acid, from which it separates rapidly on cooling, in the form of slender, colourless needles.

Generally speaking, this acid is less soluble in solvents than the isomeric $\Gamma^{cistrans}$ acid, but the difference in solubility is not sufficient to allow of the two acids being readily separated by recrystallisation. The solution of Γ^{cis} hexamethylenedicarboxylic acid in dilute carbonate of soda does not decolorise potassium permanganate even on long standing (compare Baeyer, *Annalen*, **245**, 146). The acid is, however, readily oxidised by nitric acid, although it is only slowly acted on when boiled with potassium dichromate and dilute sulphuric acid. When heated with concentrated sulphuric acid, a vigorous action sets in, with evolution of sulphurous anhydride and subsequent charring; this experiment was repeated several times in the hope that under suitable conditions isophthalic acid might be obtained, but as yet with only negative results.

The basicity of the acid was determined by titration with standard solution of potassium hydrate, using a trace of phenolphthaleïn as indicator.

0·2378 gram substance required for neutralisation 27·8 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH) = 0·1554 gram KOH.

A bibasic acid of the formula $C_8H_{12}O_4$ requires theoretically 0·1548 gram KOH.

Salts of Γ^{cis} *Hexamethylenedicarboxylic Acid.*

Silver salt, $Ag_2C_8H_{10}O_4$.—This is thrown down on the addition of silver nitrate to the warm neutral solution of the potassium salt as a white, apparently crystalline precipitate; this is collected, washed well with water, and dried, first on a porous plate over sulphuric acid in a vacuum, and then at 100°; when analysed, it gave the following result:—

I. 0·2124 gram substance gave 0·0515 gram H_2O; 0·1925 gram CO_2, and 0·1189 gram Ag.

II. 0·1640 gram substance left on ignition 0·0912 gram Ag.

	Theory. $C_8H_{10}Ag_2O_4$.	Found. I.	Found. II.	
C	24·92 per cent.	24·72	—	per cent.
H	2·59 „	2·69	—	„
Ag	55·87 „	55·93	55·61	„

This salt is exceedingly stable; it can be heated to 120° without apparent change, and is only very slowly darkened by exposure to diffused daylight; it is only sparingly soluble in water.

Calcium Salt, $C_8H_{10}O_4Ca + 3H_2O$ (?).—The preparation of this characteristic salt is given above (p. 809). The analysis of three different samples of the air-dried substance indicates that it crystallises with 3 mols. H_2O, two of which are given off at 100°, and the third at 180°.

I. The salt was exposed to the air for two days.
0·1610 gram substance, heated at 100°, lost 0·0212 gram = 13·23 per cent.

II. The salt was exposed to the air for four days.
0·1561 gram substance, heated at 100°, lost 0·0190 gram = 12·17 per cent.

III. The salt had been exposed to the air for eight days.
0·2265 gram substance, heated at 100°, lost 0·0245 gram = 10·80 per cent.

Theoretically, the salt $C_8H_{10}O_4Ca + 3H_2O$, giving off two of its three molecules of water of crystallisation, should lose 13·63 per cent. in weight; it would therefore appear from the above numbers that a portion of the water of crystallisation is gradually given off on exposure to the air at ordinary temperature.

The residues from Experiments II and III, on heating at 175° in a Victor Meyer drying oven, heated by boiling aniline, behaved as follows:—

II. 0·1371 gram substance lost 0·0112 gram = 8·17 per cent.
III. 0·2020 gram substance lost 0·0180 gram = 8·91 per cent.

$CaC_8H_{10}O_4 + H_2O$ contains 7·99 per cent. of water of crystallisation. The analysis of the salt, dried at 175° till constant, gave the following results:—

I. 0·1259 gram substance, heated with sulphuric acid, gave 0·0792 gram $CaSO_4$.

II. 0·1392 gram substance, heated with sulphuric acid, gave 0·0878 gram $CaSO_4$.

	Theory.	Found.	
	$CaC_8H_{10}O_4$.	I.	II.
Ca	19·05 per cent.	18·51	18·55 per cent.

This calcium salt crystallises in the form of slender needles, which when once deposited are only very sparingly soluble in water. A sparingly soluble calcium salt, probably identical with the above, is produced when calcium chloride is added to a strong solution of the

ammonium salt of the acid, and the mixture boiled. A neutral solution of the potassium salt of Γ^{cis} hexamethylenedicarboxylic acid, of the strength obtained by neutralising the dry acid with standard potassium hydrate solution (1 c.c. = 0·00559 gram KOH), shows the following behaviour with reagents :—

Copper sulphate, a light blue precipitate, very sparingly soluble even in boiling water. *Zinc sulphate*, no precipitate in the cold, but on boiling a slight turbidity. *Lead acetate*, a white, crystalline precipitate, which forms at once, and under the microscope is seen to consist of groups of irregularly formed needles; the precipitate is almost insoluble in boiling water. *Barium* and *calcium chlorides*, no precipitate.

Anhydride of Γ^{cis} *Hexamethylenedicarboxylic Acid.*

In the introduction to this paper, it is stated that, in view of Baeyer's deductions from his experiments on the reduction of terephthalic acid, it might be expected that Γ^{cis} hexamethylenemetadicarboxylic acid would behave like a fatty acid of similar constitution, such as glutaric acid, and, like this acid, under suitable treatment yield an anhydride. Although, at first, this Γ^{cis} acid, on account of its high melting point and other properties, was thought to be the $\Gamma^{cistrans}$ or fumaroïd form of hexamethylenedicarboxylic acid, it nevertheless seemed possible, that, when digested with acetyl chloride, this modification might be converted into the anhydride of the Γ^{cis} acid, just as fumaric acid, under similar circumstances, yields maleïc anhydride (Perkin, *Ber.*, **15**, 1073, and Anschütz, *Ber.*, **14**, 2792).

In order to test this supposition, 1 gram of the pure Γ^{cis} acid was heated in a very small flask, connected with a reflux apparatus, with excess of acetyl chloride for about one hour, the excess of acetyl chloride distilled off, and the almost colourless, oily residue transferred to a small dish and heated gently on a sand-bath till free from acetic acid. The product, which on cooling solidified to a hard mass of needle-shaped crystals, was spread on a porous plate to remove traces of oily impurity, the colourless, crystalline residue dissolved in a little boiling benzene, mixed with about an equal bulk of hot light petroleum, and allowed to cool slowly. In this way the anhydride of Γ^{cis} hexamethylenedicarboxylic acid was obtained pure in the form of magnificent, glistening, needle-shaped crystals, which, after drying at 100°, gave the following numbers on analysis :—

0·1142 gram substance gave 0·0689 gram H_2O, and 0·2604 gram CO_2.

	Theory. $C_8H_{10}O_3$.	Found.
C	62·33 per cent.	62·19 per cent.
H	6·50 „	6·70 „
O	31·17 „	31·11 „

This anhydride melts at 187—189° with slight previous softening, and distils at a high temperature almost without decomposition. It is readily soluble in benzene, acetic acid, and alcohol, excessively so in chloroform, but only sparingly in cold bisulphide of carbon and light petroleum. Hexamethylenedicarboxylic anhydride is only very slowly decomposed by cold water or cold dilute sodium carbonate solution, but it dissolves readily in hot water, and the solution, if sufficiently concentrated, deposits, on cooling, needle-shaped crystals of pure Γ^{cis} hexamethylenedicarboxylic acid (m. p. 161—163°).

Conversion of Γ^{cis} *Hexamethylenedicarboxylic Acid into* $\Gamma^{cistrans}$ *Hexamethylenedicarboxylic Acid.*

This interesting isomeric change was brought about by heating the very carefully purified Γ^{cis} acid with concentrated hydrochloric acid in a sealed tube at 180°, but as stated in the introduction the conversion is only partial, a considerable quantity of the original acid remaining unchanged. The tube, on cooling, contained a granular, crystalline mass, which melted irregularly at 135—150°, and behaved in every respect as a mixture of the Γ^{cis} and $\Gamma^{cistrans}$ acids.

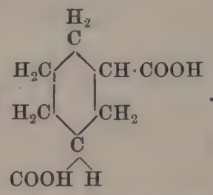
In order to prove the formation of the $\Gamma^{cistrans}$ acid, the contents of the tube was extracted four times with ether, the ethereal solution evaporated, the residue dissolved in a little water, neutralised with ammonia, heated to boiling, and gradually mixed with a large excess of a concentrated solution of calcium chloride. The heavy, white, satiny precipitate of the calcium salt of the Γ^{cis} acid thus produced was collected on a filter, washed with hot water, and decomposed with hydrochloric acid, when a quantity of a white powder was obtained, which, after recrystallisation, melted at 161—163°, and consisted of pure Γ^{cis} acid. The filtrate from the sparingly soluble calcium salt was acidified with hydrochloric acid, extracted four times with ether, the ethereal solution evaporated, the residual oil stirred with a glass rod till solid, and the solid mass spread on a porous plate to remove traces of oily impurity. In this way a white, crystalline substance was obtained, which, after two fractional crystallisations from hydrochloric acid, melted at 118—120°, and possessed all the properties of $\Gamma^{cistrans}$ hexamethylenedicarboxylic acid (see next section).

Analysis :—

0·1369 gram substance gave 0·0861 gram H_2O and 0·2789 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found.
C	55·81 per cent.	55·56 per cent.
H	6·98 „	6·98 „
O	37·21 „	37·46 „

$\Gamma^{cistrans}$ *Hexamethylenemetadicarboxylic Acid*,



The mother liquors of the sparingly soluble calcium salt of Γ^{cis} hexamethylenedicarboxylic acid (see p. 809) contain the readily soluble salt of the $\Gamma^{cistrans}$ acid, together with traces of the former salt. In order to separate the two salts as far as possible, the solutions were evaporated to a small bulk (but not to such an extent as to cause the soluble calcium salt to crystallise out), filtered from a very small quantity of a calcium salt which formed, and then evaporated to dryness. The residue was dissolved in a small quantity of boiling concentrated hydrochloric acid, the solution filtered through glass wool and vigorously stirred till a small quantity of crystals had formed, again filtered, and allowed to stand in a cool place for four hours. At the end of this time a considerable crop of crystals had separated; these were collected, washed with concentrated hydrochloric acid, recrystallised from this solvent, dried at 100°, and analysed with the following result:—

0·1344 gram substance gave 0·0863 gram H_2O and 0·2750 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found.
C	55·81 per cent.	55·81 per cent.
H	6·98 „	7·13 „
O	37·21 „	37·06 „

When heated in a capillary tube, $\Gamma^{cistrans}$ hexamethylenedicarboxylic acid melts fairly sharply at 118—120°. It is possible that, in spite of the care taken in separating and purifying this acid, it may still contain traces of Γ^{cis} hexamethylenedicarboxylic acid, and the melting point 118—120° may therefore not be quite correct. That, at the most, only traces of the acid of higher melting point are present is shown by the fact that a strong neutral solution of the $\Gamma^{cistrans}$ acid, on the addi-

tion of calcium chloride, gives no precipitate even on continued boiling.

$\Gamma^{cistrans}$ hexamethylenedicarboxylic acid resembles the Γ^{cis} acid very closely in its properties; it is, however, slightly more soluble in concentrated hydrochloric acid and other solvents than the latter acid; both acids show the same stability when treated with potassium permanganate in alkaline solution.

The basicity of the acid was determined by titration with standard potassium hydrate solution.

0·6563 gram substance required for neutralisation 76·5 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH) = 0·4275 gram KOH.

A bibasic acid, $C_8H_{12}O_4$, requires for neutralisation 0·4274 gram KOH.

Salts of $\Gamma^{cistrans}$ Hexamethylenedicarboxylic Acid.

Silver Salt, $Ag_2C_8H_{10}O_4$.—This salt was prepared by adding silver nitrate to the warm, neutral solution of the potassium salt. It is a heavy, white precipitate, sparingly soluble in water.

Dried at 100°, this salt gave the following numbers on analysis:—

I. 0·2366 gram substance gave 0·0562 gram H_2O, 0·2124 gram CO_2, and 0·1302 gram Ag.

II. 0·2711 gram substance left on ignition 0·1513 gram Ag.

III. 0·4114 „ „ 0·2301 „

	Theory. $C_8H_{10}Ag_2O_4$.	Found. I.	II.	III.	
C	24·92 p. c.	24·80	—	—	p. c.
H	2·59 „	2·66	—	—	„
Ag	55·87 „	55·69	55·81	55·93	„

This salt is very stable, and in other respects very similar to the silver salt of Γ^{cis} hexamethylenedicarboxylic acid.

A solution of the potassium salt of the strength obtained by neutralising the dry acid with standard solution of potassium hydrate (1 c.c. = 0·00559 gram KOH) shows the following behaviour with reagents:—

Copper sulphate, a light-blue precipitate sparingly soluble in water. *Zinc sulphate*, no precipitate in the cold, but, on boiling, the solution becomes slightly turbid, owing to the separation of a small quantity of a zinc salt. *Lead acetate*, at first no precipitate, but in a few seconds a beautifully crystalline lead salt separates, which under the microscope is seen to consist of minute plates; this

salt is almost insoluble in water. *Barium and calcium chlorides*, no precipitates.

Action of Acetyl Chloride on $\Gamma^{cistrans}$ *Hexamethylenedicarboxylic Acid. Conversion of this Acid into* Γ^{cis} *Hexamethylenedicarboxylic Acid.*

The formation of an anhydride from Γ^{cis} hexamethylenedicarboxylic acid by the action of acetyl chloride has been described on p. 812, and, for reasons there stated, it seemed interesting to determine whether the $\Gamma^{cistrans}$ acid under similar conditions would yield *the same anhydride*.

1 gram of pure $\Gamma^{cistrans}$ acid was digested with acetyl chloride for one hour, the excess of the reagent removed by evaporation, and the residual solid, crystalline substance purified by spreading it on a porous plate and subsequently recrystallising it from a mixture of benzene and light petroleum. In this way a beautiful, colourless, crystalline substance was obtained which melted at 187—189°, and in its other properties proved to be identical with the anhydride of Γ^{cis} hexamethylenedicarboxylic acid. Analysis:—

0·1063 gram substance gave 0·0629 gram H_2O and 0·2413 gram CO_2.

	Theory. $C_8H_{10}O_3$.	Found.
C	62·33 per cent.	61·90 per cent.
H	6·50 „	6·59 „
O	31·17 „	31·51 „

The yield of anhydride obtained in this experiment seemed to be quantitative. As, furthermore, this anhydride when dissolved in water yields Γ^{cis} hexamethylenedicarboxylic acid, it follows that the above method can be used as a means of converting the $\Gamma^{cistrans}$ acid quantitatively into the Γ^{cis} acid, whereas the conversion by means of hydrochloric acid, as described in the next section, is always incomplete.

The anhydride which is thus obtained by the action of acetyl chloride on both isomeric hexamethylenedicarboxylic acids is characterised by an extraordinary capacity for crystallising, and this property may be made use of with great advantage as a means of purifying very crude residues of the mixed acids, from which otherwise nothing crystalline could be isolated. These residues, such as washings of beakers and filter-papers, aqueous extracts of pieces of porous plate, which have been used in the purification of the acids as described in this paper, are first treated with calcium carbonate, and roughly separated into the calcium salts of the Γ^{cis} and $\Gamma^{cistrans}$ acids;

the crude acids obtained from the calcium salts are converted into the anhydride, and this substance, which if very impure will not directly solidify, dissolved in benzene and cautiously mixed with light petroleum. On standing, the anhydride separates in long crystals, and is readily purified, except in exceptional cases, when distillation under reduced pressure and subsequent recrystallisation must be resorted to.

Conversion of $\Gamma^{cistrans}$ *Hexamethylenedicarboxylic Acid into* Γ^{cis} *Hexamethylenedicarboxylic Acid by means of Hydrochloric Acid.*

One of the most interesting facts which have been noticed in this investigation is that the two isomeric hexamethylenedicarboxylic acids, when heated with hydrochloric acid at 180°, are each to some extent converted into the other, and thus, no matter which acid you start with, the product of the reaction is sure to consist of this acid mixed with an apparently definite quantity of its isomer. The isomeric change in the case of Γ^{cis} hexamethylenedicarboxylic acid has been described on p. 813, and it is therefore only necessary to show that a similar change takes place in the case of the $\Gamma^{cistrans}$ acid. For this purpose, about 1 gram of $\Gamma^{cistrans}$ hexamethylenedicarboxylic acid (m. p. 118—120°) was heated in a sealed tube with 15 c.c. of concentrated hydrochloric acid for three hours at 180°, and the crystals which separated from the concentrated solution, on cooling, collected, washed with hydrochloric acid, and dried at 100°. These crystals melted irregularly from 140—155°, and obviously contained a small quantity of unchanged $\Gamma^{cistrans}$ acid; the experiment was therefore repeated, and the action of the hydrochloric acid continued for eight hours, but the resulting acid still showed no sharp melting point. The whole was now dissolved in ammonia solution, the excess of ammonia expelled by boiling, a strong solution of calcium chloride added to the hot solution, and the copious precipitate which formed collected, washed with water, decomposed by hydrochloric acid, and the resulting acid recrystallised from this solvent. In this way a considerable quantity of Γ^{cis} hexamethylenedicarboxylic acid was obtained which melted at 159—161°, and gave the following results on analysis :—

0·1222 gram substance gave 0·0785 gram H_2O and 0·2497 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found.
C	55·81 per cent.	55·73 per cent.
H	6·98 „	7·03 „
O	37·21 „	37·24 „

As nearly as could be judged in a small experiment, about 60 per cent. of the $\Gamma^{cistrans}$ acid is converted into the Γ^{cis} acid by this treatment. At the same time it should be mentioned that the unchanged acid was not isolated and analysed, but only roughly identified as such.

Heriot Watt College, Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

New Synthesis of the Hexamethylenedicarboxylic Acids.

By W. H. Perkin, Jun., Ph.D., F.R.S., and Bertram Prentice.

In the last number of this Journal (p. 798), it was shown that the sodium compound of ethyl pentanetetracarboxylate reacts with methylene iodide in alcoholic solution at 100°, with formation of ethyl hexamethylenetetracarboxylate, thus:—

$$H_2C\begin{<}CH_2\cdot CNa(COOC_2H_5)_2\\CH_2\cdot CNa(COOC_2H_5)_2\end{>} + CH_2I_2 = H_2C\begin{<}CH_2\cdot C(COOC_2H_5)_2\\CH_2\cdot C(COOC_2H_5)_2\end{>}CH_2 + 2NaI.$$

On hydrolysis, this ethereal salt yields the corresponding hexamethylenetetracarboxylic acid, and the latter, when heated at 200—220°, is decomposed with elimination of 2 mols. of CO_2. and formation of Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenemetadicarboxylic acids:—

$$H_2C\begin{<}CH_2\cdot C(COOH)_2\\CH_2\cdot C(COOH)_2\end{>}CH_2 = H_2C\begin{<}CH_2\cdot CH\cdot COOH\\CH_2\cdot CH\cdot COOH\end{>}CH_2 + 2CO_2.$$

As the amount of these interesting acids obtained by this method is small, numerous experiments were made, under very varying conditions, with the object of improving the yield, but without success. It then seemed probable that the same ethyl hexamethylenetetracarboxylate should result from the action of trimethylene bromide on the disodium compound of ethyl propanetetracarboxylate, thus:—

$$(COOC_2H_5)_2{\cdot}CNa{\cdot}CH_2{\cdot}CNa(COOC_2H_5)_2 + BrCH_2{\cdot}CH_2{\cdot}CH_2Br = \begin{matrix}(COOC_2H_5)_2C{-}CH_2{-}C(COOC_2H_5)_2\\ \quad\quad\quad\

and extracted three times with ether. During this operation, beautiful, yellow crystals separated from the ethereal solution; they contain sodium, and consist apparently of the sodium compound of a somewhat complicated ethereal salt; this substance, which seems to have very interesting properties, is at present under examination. The filtrate from this sodium compound, after drying over calcium chloride and evaporating the ether, deposited a thick oil, which was purified by fractional distillation under reduced pressure, and thus separated into unchanged ethyl malonate, and a substance boiling at 230—240° (80 mm.), which, after refractionation, boiled constantly at 234—236° (80 mm.), and was found to consist of pure ethyl propanetetracarboxylate.

0·2016 gram substance gave 0·1354 gram H_2O and 0·4020 gram CO_2.

	Theory. $C_{15}H_{24}O_8$.	Found.
C	54·21 per cent.	54·35 per cent.
H	7·23 „	7·46 „
O	38·55 „	38·19 „

The yield obtained was about 60 per cent. of the theoretical, without taking the recovered ethyl malonate into account.

The action of methylene chloride on the sodium compound of ethyl malonate has been already investigated by S. Tanatar (*Chem. Centralblatt*, 1891, i, 21, 22), but his results differ entirely from those described above, as he makes no mention of having obtained an ethereal salt, $C_{15}H_{24}O_8$. On this account it seemed necessary to prove that the ethereal salt, $C_{15}H_{24}O_8$, obtained by this reaction, really was ethyl propanetetracarboxylate before employing it for synthetical experiments. This is readily done by converting it into the corresponding tetracarboxylic acid, and then decomposing this by heating it at 200°, when glutaric acid results (compare W. H. Perkin, jun., Guthzeit and Dressel, *loc. cit.*).

$$(COOH)_2CH{\cdot}CH_2{\cdot}CH(COOH)_2 = COOH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOH + 2CO_2.$$

30 grams of the pure ethyl salt, $C_{15}H_{24}O_8$, was dissolved in methyl alcohol, mixed with a solution of 25 grams of potassium hydrate in methyl alcohol, and the whole heated for three hours on a water-bath, in a flask connected with a reflux apparatus. The product was then mixed with water, vigorously boiled till free from alcohol, evaporated to a small bulk, acidified with hydrochloric acid, and extracted 10 times with pure ether. The ethereal solution was dried over calcium chloride, evaporated, and the residual, yellowish, semi-

solid mass heated at 200—220° until the evolution of carbonic anhydride had entirely ceased.

In order to purify the crude acid thus obtained, the residual dark-brown syrup was dissolved in 10 times its weight of absolute alcohol, the solution mixed with 1/5th of the quantity of concentrated sulphuric acid, heated in a reflux apparatus for two hours, and the ethereal salt isolated by pouring the product into water and extracting with ether. The ethereal solution was well washed with water, dried over calcium chloride, evaporated, and the crude ethyl salt purified by fractional distillation. In this way a colourless oil was obtained, which boiled constantly at 234°, and showed all the properties of ethyl glutarate. Analysis:—

0·1104 gram substance gave 0·0864 gram H_2O and 0·2321 gram CO_2.

	Theory. $COOC_2H_5{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}COOC_2H_5$.	Found.
C	57·44 per cent.	57·34 per cent.
H	8·51 „	8·68 „
O	34·05 „	33·98 „

The pure ethereal salt was hydrolysed by boiling with an excess of alcoholic potash for two hours, the solution mixed with water, boiled until free from alcohol, acidified with hydrochloric acid, and extracted five times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a crystalline cake of almost pure glutaric acid; this was washed with ether, dried on a porous plate over sulphuric acid, under reduced pressure, and then at 80°.

The acid melted at 97—98°, and on analysis gave numbers agreeing with those required for glutaric acid.

0·1702 gram substance gave 0·0950 gram H_2O and 0·2836 gram CO_2.

	Theory. $C_5H_8O_4$.	Found.
C	45·45 per cent.	45·48 per cent.
H	6·06 „	6·20 „
O	48·48 „	48·32 „

The formation of this acid proves that the substance $C_{15}H_{24}O_8$, obtained by the action of methylene chloride on the sodium compound of ethyl malonate, is in reality ethyl propanetetracarboxylate, $(COOC_2H_5)_2CH{\cdot}CH_2{\cdot}CH(COOC_2H_5)_2$.

The method of preparation of glutaric acid given above is probably the simplest and cheapest way of preparing this important substance, and, with this object in view, it would not be necessary to purify the ethyl propanetetracarboxylate by fractionation, the crude product of the action of methylene chloride on the sodium compound of ethyl malonate, might be freed from unchanged ethyl malonate by distilla-

tion in a current of steam, and the residual oil at once hydrolysed and treated as above.

Action of Trimethylene Bromide on the Disodium Compound of Ethyl Propanetetracarboxylate. Formation of Hexamethylenetetracarboxylic Acid.

In carrying out this synthesis, 70 grams of pure ethyl propanetetracarboxylate was mixed with a solution of 9·7 grams of sodium in 120 grams of absolute alcohol, 43 grams of trimethylene bromide added, and the whole heated gently in a flask connected with a reflux apparatus. In a short time, the temperature rose rapidly, a vigorous reaction set in, and, after boiling for about one hour, the decomposition was completed. The product was gently evaporated till free from alcohol, mixed with water, extracted two or three times with ether, the ethereal solution evaporated, and the residual oil (78 grams) hydrolysed by boiling with $1\frac{1}{2}$ times the calculated quantity of alcoholic potash for three hours. After mixing with water, the alkaline solution was boiled until free from alcohol, evaporated to a small bulk, acidified with hydrochloric acid, and extracted 25 times with pure ether. The ethereal solution, after drying over calcium chloride and evaporating to a small bulk, deposited, on standing, a quantity of a white, crystalline substance; this was collected, washed with ether, and recrystallised from warm water.

In this way, beautiful, colourless, glistening crystals were obtained, which, on analysis, proved to be pure hexamethylenetetracarboxylic acid:—

0·1418 gram substance gave 0·0620 gram H_2O and 0·2400 gram CO_2.

	Theory. $C_{10}H_{12}O_8$.	Found.
C	46·15 per cent.	46·15 per cent.
H	4·61 „	4·85 „
O	49·23 „	49·00 „

This substance, when rapidly heated, decomposed at 218—220°, and was in all respects identical with the hexamethylenetetracarboxylic acid previously obtained. A quantity of the pure acid was heated at 220° until the evolution of carbonic anhydride had ceased, and the resulting, almost colourless oil which consists of a mixture of Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenemetadicarboxylic acids, digested with acetyl chloride, and thus converted into the anyhdride of the Γ^{cis} acid (this vol., pp. 812, 816). The solid, crystalline mass which remained after distilling off the excess of the acetyl chloride and the acetic

acid was purified by spreading on a porous plate, and subsequen recrystallisation from a mixture of benzene and light petroleum.

The magnificent, glistening crystals thus obtained, after drying at 110°, melted at 187°, and consisted of the pure anhydride of Γ^{cis} hexamethylenemetadicarboxylic acid, as is shown by the following analyses:—

I. 0·1074 gram substance gave 0·0656 gram H_2O and 0·2451 gram CO_2.

II. 0·1599 gram substance gave 0·0958 gram H_2O and 0·3642 gram CO_2.

	Theory. $C_8H_{10}O_3$.	Found. I.	II.
C.....	62·33 per cent.	62·24	62·11 per cent.
H.....	6·50 „	6·79	6·65 „
O.....	31·17 „	30·97	31·24 „

This anhydride was further identified by conversion into Γ^{cis} hexamethylenemetadicarboxylic acid by boiling with water.

The ethereal mother liquors from which the hexamethylenetetracarboxylic acid had separated, as described above, were evaporated, the residue heated at 200—220° until the evolution of carbonic anhydride had ceased, and then converted into the methyl salt by means of methyl alcohol and sulphuric acid (*loc. cit.*, p. 806).

On fractioning this salt, a small amount of crude methyl hexamethylenedicarboxylate was obtained, boiling at 170—185° (60 mm.), together with considerable quantities of high and low boiling fractions; of these, the former were not examined; the latter appear to contain methyl glutarate, which must have been produced by the hydrolysis of some unchanged ethyl propanetetracarboxylate.

The yield of pure hexamethylenetetracarboxylic acid obtained in the above reaction from 140 grams of ethyl propanetetracarboxylate was about 13·5 grams, or about 12 per cent. of the theoretical. The amount of hexamethylenedicarboxylic acids obtained by the hydrolysis of the methyl salt has not yet been accurately determined, but it is approximately 4 grams.

Further experiments on these interesting acids are in progress.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Synthesis of Hexahydroterephthalic Acid.

By J. E. Mackenzie, B.Sc., and W. H. Perkin, Jun., Ph.D., F.R.S.

In a paper published a short time since (Trans., 1891, **59**, 798), it was shown that the disodium compound of ethyl pentanetetracarboxylate, when digested in alcoholic solution with methylene iodide at 100° is, in part, converted into ethyl hexamethylene tetracarboxylate [1 : 1 : 3 : 3], thus :—

$$H_2C<\begin{matrix}CH_2\cdot CHNa(COOC_2H_5)_2\\CH_2\cdot CHNa(COOC_2H_5)_2\end{matrix} + CH_2I_2 =$$

$$H_2C<\begin{matrix}CH_2\cdot C(COOC_2H_5)_2\\ \\CH_2\cdot C(COOC_2H_5)_2\end{matrix}>CH_2 + 2NaI.$$

The same ethereal salt is also produced by the action of trimethylene bromide on the disodium compound of ethyl propanetetracarboxylate,

$$(COOC_2H_5)_2CNa\cdot CH_2\cdot CNa(COOC_2H_5)_2 + BrCH_2\cdot CH_2\cdot CH_2Br =$$

$$\begin{matrix}(COOC_2H_5)_2C-CH_2-C(COOC_2H_5)_2\\ \quad\quad\quad\

isomeric Γ^{cis} and $\Gamma^{cistrans}$ hexamethylenemetadicarboxylic acids (hexahydroisophthalic acids), with elimination of 2 mols. of carbonic anhydride, thus:—

$$H_2C\begin{cases}CH_2\cdot C(COOH)_2\\ \quad >CH_2\\ CH_2\cdot C(COOH)_2\end{cases} = H_2C\begin{cases}CH_2\cdot CH\cdot COOH\\ \quad >CH_2\\ CH_2\cdot CH\cdot COOH\end{cases} + 2CO_2.$$

During the course of the experiments, it was thought probable that the two isomeric hexahydroterephthalic acids,

$$COOH\cdot CH<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH\cdot COOH,$$

which Baeyer prepared in the course of his beautiful investigations on the reduction of terephthalic acid (*Annalen*, **245**, 169—174), might be synthetically produced in a similar way, from the ethereal salt formed by the interaction of the disodium compound of ethyl butanetetracarboxylate with ethylene bromide, thus:—

I. $(COOC_2H_5)_2CNa\cdot CH_2\cdot CH_2\cdot CNa(COOC_2H_5)_2 + BrCH_2\cdot CH_2Br$

$$= (COOC_2H_5)_2C<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>C(COOC_2H_5)_2 + 2NaBr.$$

Ethyl hexamethylenetetracarboxylate [1 : 1 : 4 : 4].

II. $(COOH)_2C<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>C(COOH)_2 =$

Hexamethylenetetracarboxylic acid.

$$COOH\cdot CH<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH\cdot COOH + 2CO_2.$$

Hexahydroterephthalic acid.

On making the experiment, it was found that a considerable quantity of the sparingly soluble $\Gamma^{cistrans}$ hexahydroterephthalic acid was produced in this way, and from the mother liquors of this acid a small quantity of an acid melting at 159—162° was with difficulty isolated; the latter is probably the corresponding Γ^{cis} acid, which melts at 161—162°. Unfortunately, it was not possible to obtain sufficient of the second acid for analysis, owing to the difficulty of preparing ethyl butanetetracarboxylate in large quantities.

This ethereal salt, the preparation of which has been given in a previous paper (Trans., 1887, **51**, 19), is produced in very small quantities when ethylene bromide acts on the sodium compound of ethyl malonate, thus:—

$$2(COOC_2H_5)_2CHNa + BrCH_2\cdot CH_2Br =$$
$$(COOC_2H_5)_2CH\cdot CH_2\cdot CH_2\cdot CH(COOC_2H_5)_2 + 2NaBr;$$

but, in spite of numerous experiments instituted with the object of improving the yield, the largest amount which has as yet been obtained was 35 grams from 1 kilo. of ethyl malonate. For this reason, it was not possible to follow the course of the reaction between the disodium compound of this ethereal salt and ethylene bromide through all its stages, as was the case in the experiments on the synthetical formation of the hexahydroisophthalic acids.

The synthesis of hexahydroterephthalic acid was carried out briefly as follows:—

4 grams of sodium was dissolved in 60 grams of absolute alcohol; the well-cooled solution mixed with 30 grams of pure ethyl butane-tetracarboxylate, 17 grams of ethylene bromide added, and the whole heated in a soda-water bottle at 100° for 10 hours.

The product, which was brownish, and smelt distinctly of ethylene bromide, still had a strongly alkaline reaction; it was mixed with water, extracted four times with ether, the ethereal solution washed well with water, dried over calcium chloride, evaporated, and the residual brownish oil (23 grams) hydrolysed by boiling with a mixture of concentrated sulphuric acid (1 part), water (1 part), and glacial acetic acid (2 parts) for six hours in a reflux apparatus. Steam was next passed through the boiling liquid until all the acetic acid had been removed, the pale-brownish solution cautiously concentrated on a water-bath, and then extracted 30 times with ether. The ethereal solution, after being dried over calcium chloride and evaporated, left 12 grams of a thick, oily acid, which, on standing over sulphuric acid under diminished pressure, rapidly deposited crystals; these, after washing with ether, in which they are sparingly soluble, crystallise from water in cauliflower-like masses, which melt approximately at 152—153°.

The results of the analysis indicate that this substance is hexamethylenetricarboxylic acid,

$$COOH\cdot CH<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>C(COOH)_2.$$

0·1410 gram substance gave 0·0800 gram H_2O and 0·2572 gram CO_2.

	Theory. $C_9H_{12}O_6$.	Found.
C.....	50·00 per cent.	49·75 per cent.
H	5·55 „	6·30 „
O.....	44·44 „	43·95 „

Owing to the small amount of material at our disposal, no further experiments could be made with this acid, and for this reason, it

must in the meantime remain doubtful whether this view of the constitution of this substance is correct.

The remainder of the crude acid was heated at 200—220°, until all evolution of carbonic anhydride had ceased, and the thick, brownish residue, which became almost solid even while quite hot, was allowed to remain in contact with a porous plate for some days; it was then dissolved in dilute sodium carbonate solution, and digested with freshly ignited animal charcoal for two or three hours. The filtered solution after evaporating to a small bulk, and acidifying with hydrochloric acid, deposited on standing about 1·3 grams of a granular precipitate; this, on examination, was found to consist of almost pure $\Gamma^{cis trans}$ hexahydroterephthalic acid. The substance, after recrystallisation from water, gave the following numbers on analysis:—

0·1434 gram substance gave 0·0920 gram H_2O and 0·2933 gram CO_2.

	Theory. $C_8H_{12}O_4$.	Found.
C	55·81 per cent.	55·77 per cent.
H	6·98 „	7·12 „
O	37·21 „	37·11 „

This acid melts approximately at 300°, but not sharply; when strongly heated, it sublimes, and this behaviour was especially well observed during the combustion of the substance, when almost the whole sublimed and was deposited in glistening crystals on the cooler portions of the tube. It is readily soluble in warm water, but much more sparingly in cold water; the solution of the sodium salt of the acid does not decolorise potassium permanganate even on standing for some time.

In order, however, to prove conclusively that this acid was identical with the $\Gamma^{cis trans}$ hexahydroterephthalic acid obtained by Baeyer from terephthalic acid, the methyl salt was prepared according to Baeyer's directions.

About 0·2 gram of the acid was gently heated in a test-tube with an excess of phosphorus pentachloride for a few seconds, allowed to cool, and the residual solid mass mixed with methyl alcohol. The product was poured into water, the crystalline mass which separated collected, washed with water, and dried on a porous plate over sulphuric acid under diminished pressure. The resulting glistening, crystalline mass melted at 66—68°, and after recrystallisation from light petroleum at 69—70°; Baeyer gives 71° as the melting point of the dimethyl salt of $\Gamma^{cis trans}$ hexahydroterephthalic acid.

The mother liquors from the above acid were evaporated to a very small bulk, allowed to stand for some days, the crystalline mass which

separated, collected, washed with a little water, and dried on a porous plate at 100°. The resulting crude substance, which, when heated in a capillary tube, began to melt at 145°, and was not completely melted at 190°, was separated into three substances by conversion into the calcium salt, and repeated recrystallisation of the acids from water: that is, into small quantities of $\Gamma^{cistrans}$ hexahydroterephthalic acid, a considerable quantity of an acid melting at 147—149°, probably adipic acid (from the hydrolysis of some unchanged ethyl butanetetracarboxylate), and about 0·028 gram of an acid melting at 159—162°, which is probably $\Gamma^{cistrans}$ hexahydroterephthalic acid (m. p. 161—162°).

The titration of this acid gave the following results:—

0·0271 gram required for neutralisation 3·1 c.c. of potassium hydrate solution (1 c.c. = 0·00559 gram KOH) = 0·0173 gram KOH.

A bibasic acid of the formula $C_8H_{12}O_4$ requires theoretically 0·0177 gram KOH.

The solution of the potassium salt of this acid, rendered slightly alkaline by the addition of potassium carbonate, did not decolorise potassium permanganate solution.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Acetylcarbinol.

By W. H. Perkin, Jun., Ph.D., F.R.S.

Although several members of the series of ketone alcohols have been isolated and described, it is surprising, in view of the great interest attaching to these compounds, that the first member of the series, acetylcarbinol (acetol, acetone alcohol), $CH_3 \cdot CO \cdot CH_2 \cdot OH$, has hitherto been obtained only in aqueous solution.

In this form it has been obtained by the following reactions:—

1. When α-chlorallyl alcohol, $CH_2 : CCl \cdot CH_2 \cdot OH$, is dissolved in concentrated sulphuric acid, and the product distilled in a current of steam, a dilute aqueous solution of acetylcarbinol passes over (Henry, *Bl.*, **39**, 526).

2. When caustic potash is added to fused cane sugar or grape sugar in a retort, an aqueous distillate is obtained which contains acetylcarbinol (Emmerling and Lodges, *Ber.*, **16**, 837).

3. When monobromacetone, $CH_2Br \cdot CO \cdot CH_3$, is treated in aqueous solution with silver oxide, acetylcarbinol is formed. By the action of potassium carbonate on monobromacetone, Emmerling and Wagner (*Annalen*, **204**, 40) obtained a sweet substance, which was very soluble in water, reduced Fehling's solution, and which these authors supposed to be acetylcarbinol.

I have carefully repeated this latter experiment under very varied conditions, but, although I obtained a substance closely resembling the product described by Emmerling and Wagner, it was, certainly, not acetylcarbinol, as it did not distil without decomposition, and, on

analysis, numbers were obtained which differed widely from those required by the formula $CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH$.

Although acetylcarbinol itself has not been isolated, derivatives of this alcohol are well known; thus alkyl ethers of acetylcarbinol have been prepared from the corresponding propargyl compounds (Henry, *J.*, 1881, 506) by hydration by means of mercuric bromide, thus:—

$$CH{:}C{\cdot}CH_2{\cdot}OC_2H_5 + H_2O = CH_3{\cdot}CO{\cdot}CH_2{\cdot}OC_2H_5;$$

and acetylcarbinyl acetate, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}O{\cdot}C_2H_3O$, was long ago prepared by the same chemist (*Ber.*, **5**, 966), and by Zincke and Breuer (*Ber.*, **13**, 638), by digesting monochloracetone with potassium acetate in alcoholic solution:

$$CH_3{\cdot}CO{\cdot}CH_2Cl + CH_3{\cdot}COOK = CH_3{\cdot}CO{\cdot}CH_2{\cdot}O{\cdot}C_2H_3O + KCl.$$

Latterly, Laubmann (*Annalen*, **243**, 244—248) has shown that solutions of acetylcarbinol, when treated with phenylhydrazine, yield an oily hydrazine compound, which, when heated with excess of the reagent, is converted into acetolosazone,

$$CH_3{\cdot}C(N_2H{\cdot}C_6H_5){\cdot}CH(N_2H{\cdot}C_6H_5).$$

The formation of this substance, which is identical with the phenylhydrazine compound of methylglyoxal, $CH_3{\cdot}CO{\cdot}COH$ (v. Pechmann, *Ber.*, **20**, 2543), proved conclusively the presence of acetylcarbinol in these solutions.

The difficulty experienced in obtaining acetylcarbinol by the hydrolysis of any of its compounds is due, in the first place, to the readiness with which it undergoes change when treated with reagents; and, secondly, to its extreme solubility in water, which renders extraction with ether or other solvents almost impossible, even in the case of moderately strong solutions.

In the course of a long series of experiments on the isolation of acetylcarbinol, extending over a number of years, it occurred to me that if chloracetone was boiled with water and some substance, such as barium carbonate, which, while capable of exercising a hydrolytic action, would, on account of its insolubility in water, be incapable of further action on the acetylcarbinol formed, very strong solutions of acetylcarbinol might be prepared from which the alcohol could be isolated by extraction with ether, thus:—

$$2CH_3{\cdot}CO{\cdot}CH_2Cl + BaCO_3 + H_2O = 2CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH + BaCl_2 + CO_2.$$

This method was investigated by Dr. J. B. Tingle and myself, and small quantities of acetylcarbinol were actually obtained in this way;

but the yield was so small, and the isolation of the product so tedious, that at that time no further experiments were made on the subject.

On resuming the investigation, it was discovered that the hydrolysis of acetylcarbinyl acetate by means of water and barium carbonate took place much more readily than that of chloracetone, and, further, that dilute solutions of acetylcarbinol could be concentrated by distillation; taking advantage of these two facts, a method was devised by which large quantities of acetylcarbinol can be obtained in a comparatively short space of time.

This method, which is described in detail in this paper, is briefly as follows:—Acetylcarbinyl acetate is boiled in aqueous solution with barium carbonate until completely hydrolysed, the resulting product freed from barium acetate by distillation under reduced pressure, and the strong aqueous solution of acetylcarbinol thus obtained separated from the bulk of the water by careful fractionation. In this way nearly the whole of the water may be removed, and the resulting 90 per cent. acetylcarbinol, after drying over anhydrous sodium sulphate, and distillation under reduced pressure, can be readily obtained pure.

Acetylcarbinol is a peculiarly smelling, colourless oil which boils at 147°, and solidifies at low temperatures; it is miscible in all proportions with water; it reduces ammoniacal solution of nitrate of silver and Fehling's solution in the cold; sodium amalgam converts it quantitatively into methyl glycol:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH + H_2 = CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH.$$

I hope at a future date to communicate to the Society the results of further experiments on this interesting substance.

Acetylcarbinyl Acetate, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}O{\cdot}C_2H_3O$.

This substance has already been prepared by Henry (*Ber.*, **5**, 966), and by Zincke and Breuer (*Ber.*, **13**, 638); it is readily produced by digesting monochloracetone with potassium acetate in alcoholic solution:

$$CH_3{\cdot}COOK + CH_3{\cdot}CO{\cdot}CH_2Cl = CH_3{\cdot}CO{\cdot}CH_2{\cdot}O{\cdot}C_2H_3O + KCl.$$

In preparing large quantities of acetylcarbinyl acetate, the method employed was that recommended by Zincke and Breuer, but slightly modified, in order to produce as large a yield as possible.

200 grams of pure, dry potassium acetate was mixed with about twice its weight of absolute alcohol, 185 grams of monochloracetone added, and the mixture heated on a water-bath in a flask connected with a reflux apparatus for two hours. After standing for 12 hours,

the product was separated from the precipitated potassium chloride by filtration on a filter-pump, the residue washed two or three times with small quantities of absolute alcohol, and the dark-coloured alcoholic liquors slowly distilled until the greater bulk of the alcohol had been removed; it was then rapidly distilled, under a pressure of 150 mm., from a strong, round-bottomed flask, heated by means of an oil-bath, until no more oily drops passed over. This method is far preferable to that recommended by Zincke and Breuer, namely, mixing the residue with water after distilling off the alcohol, and extracting with ether, as the acetate is not only miscible with water and difficult to extract by ether, but it is also, to a considerable extent, decomposed by solution in water, and great loss, therefore, occurs.

The crude acetylcarbinyl acetate, obtained by the above method, is readily purified by fractional distillation, first under reduced pressure, and then at the ordinary pressure.

Pure acetylcarbinyl acetate boils at 174—175° under a pressure of 760 mm., and at 137—138° under a pressure of 230 mm. Two specially purified preparations gave, on analysis, the following numbers:—

I. 0·1540 gram substance gave 0·0972 gram H_2O and 0·2913 gram CO_2.

II. 0·2402 gram substance gave 0·1473 gram H_2O and 0·4538 gram CO_2.

	Theory. $C_5H_8O_3$.	Found. I.	Found. II.
C	51·72 per cent.	51·57	51·50 per cent.
H	6·90 „	7·01	6·81 „
O	41·38 „	41·42	41·69 „

If the materials used in the above method of preparation are carefully dried, and precautions are taken to exclude moisture in the subsequent purification of the crude product, the yield obtained is about 80—85 per cent. of the theoretical; and this yield may be still further improved by using the alcohol from one operation for a subsequent preparation, as the small quantities of the acetate which always distil over with the alcohol may in this way be recovered.

Acetylcarbinyl acetate is a colourless, limpid liquid possessing a peculiar, sickly odour; it is miscible with water, and to some extent decomposed by it; the aqueous solution, on standing, acquires a very acid reaction. The density and magnetic rotation of this substance were determined by W. H. Perkin, sen., with the following results:—

Density:—$d\,4°/4° = 1·0912$; $d\,10°/10° = 1·0849$; $d\,15°/15° = 1·0803$; $d\,20°/20° = 1·0760$; $d\,25°/25° = 1·0719$.

Magnetic Rotation.

	t.	Sp. rotation.	Mol. rotation.
	15·2°	0·9091	5·424
	13·2	0·9150	5·458
	13·0	0·9091	5·418
	13·0	0·9076	5·409
	13·0	0·9091	5·418
	13·5	0·9091	5·416
	13·0	0·9137	5·440
	13·0	0·9113	5·426
Average ..	13·4	0·9105	5·426

The theoretical magnetic rotation of acetylcarbinyl acetate may be calculated thus:—

Acetylcarbinyl acetate results from the substitution of one of the hydrogen atoms in acetone by the group $CH_3{\cdot}COO$.

The value of this group replacing an atom of hydrogen may be deduced as follows:—

I. Magnetic rotation of octyl acetate	10·601
Magnetic rotation of octane (cal.).....	8·692
Difference = Magnetic rotation of the group $CH_3{\cdot}COO$, replacing hydrogen	1·909
II. Magnetic rotation of propyl acetate	5·487
Magnetic rotation of propane (cal.)	3·577
Difference = Magnetic rotation of the group $CH_3{\cdot}COO$, replacing hydrogen	1·910

If now we add this value to the magnetic rotation of acetone = 3·514, we obtain 5·424 as the theoretical magnetic rotation of acetylcarbinyl acetate, a number which agrees very closely with that actually found, namely, 5·426.

Acetylcarbinol, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH$.

In order to prepare acetylcarbinol from its acetate, numerous experiments were made with various hydrolysing agents under the most varied conditions, but it was soon discovered that most of these were worthless, on account of their decomposing action on the acetylcarbinol produced.

The best results were obtained with moist barium carbonate, and

ultimately the following method, which I give in detail, was adopted as giving a very satisfactory yield of the ketone alcohol :—

160 grams of pure acetylcarbinyl acetate is dissolved in 300 c.c. of water, heated to boiling in a round-bottomed flask connected with a reflux apparatus, and pure, dry barium carbonate added, advantageously in the form of small pellets, in such a way that no further addition is made until the previous pellet has entirely dissolved. At the end of about three hours the reaction is complete, as is shown by the fact that the addition of a small quantity of barium carbonate to the boiling liquid causes no further evolution of carbonic anhydride. The product is filtered from any trace of undissolved barium carbonate, and distilled as rapidly as possible, under a pressure of 100 mm., from a round-bottomed flask, heated by means of a paraffin-bath, until no more liquid passes over, but care must be taken not to raise the temperature of the bath unnecessarily high, otherwise the residue in the flask, which still contains a considerable quantity of acetylcarbinol, and the treatment of which is described below, is apt to be decomposed.

The colourless distillate, which measures about 350 c.c., when tested with Fehling's solution, as described on p. 794, is found to contain about 15 per cent. of acetylcarbinol, or about 51 grams in all.

The residue in the distilling flask is dissolved in a little water and distilled in a rapid current of steam, the paraffin-bath being kept at about 120°.

The following table may serve as an example of the distillates collected, and the amount of acetylcarbinol contained in each as determined by titration :—

	Distillate collected.	Fehling's solution reduced by 2 c.c.	Percentage of acetylcarbinol.	Total amount of acetylcarbinol.
I ..	150 c.c.	38·5 c.c.	11·5	17·2 grams.
II ..	104 „	25·3 „	7·6	7·9 „
III ..	100 „	19·5 „	6·0	6·0 „
IV ..	280 „	11·0 „	3·3	9·2 „
V ..	210 „	5·5 „	1·7	3·5 „
			Total ..	43·8 grams.

The total amount of acetylcarbinol obtained from 160 grams of acetylcarbinyl acetate was therefore approximately 94 grams, whereas theoretically it should have been 103 grams ; the hydrolysis by means of moist barium carbonate may therefore be considered as nearly quantitative.

In preparing large quantities of acetylcarbinol, the treatment of

the aqueous solutions obtained as described above was approximately as follows:—

All the solutions containing from 6—7 per cent. of acetylcarbinol were first very slowly distilled from a large, round-bottomed flask fitted with a very long colonna, until the residue on titration was found to contain from 9 to 10 per cent. of the ketone alcohol. This residue was then mixed with other solutions of the same strength and the concentration continued until ultimately a residue was obtained which contains over 90 per cent. of acetylcarbinol.

In one series of experiments, in which 1 kilo. of pure acetylcarbinyl acetate was employed, the concentration of the aqueous solutions took about 14 days, and upwards of 450 grams of 90—95 per cent. acetylcarbinol was obtained, together with large quantities of weak solutions. These weak solutions, when they contain less than 5 per cent. of acetylcarbinol, are best employed, instead of water, in decomposing fresh quantities of acetylcarbinyl acetate, as their concentration is not profitable.

In order to prepare pure acetylcarbinol, the 90—95 per cent. product is dissolved in pure ether, the ethereal solution allowed to stand over anhydrous sodium sulphate for 24 hours, filtered, the ether slowly distilled off, and the residue fractioned under reduced pressure. Almost the whole passes over between 90° and 105°, under a pressure of 150 mm., at the first distillation, leaving, however, always a small residue in the retort, and on repeated fractionation pure acetylcarbinol is readily obtained boiling constantly at 96—97° (150 mm.).

The following results were obtained on analysis:—

I. 0·1383 gram substance gave 0·1026 gram H_2O and 0·2460 gram CO_2

II. 0·2081 gram substance gave 0·1539 gram H_2O and 0·3690 gram CO_2.

III. 0·1614 gram substance gave 0·1180 gram H_2O and 0·2890 gram CO_2.

IV. 0·1890 gram substance gave 0·1390 gram H_2O and 0·3400 gram CO_2.

V. 0·1700 gram substance gave 0·1244 gram H_2O and 0·3050 gram CO_2.

	Theory. $C_3H_6O_2$	Found. I.	II.	III.	IV.	V.
C	48·65 p. c.	48·51	48·36	48·83	49·05	48·93 p. c.
H	8·10 „	8·24	8·21	8·12	8·17	8·13 „
O	43·24 „	43·25	43·43	43·05	42·78	42·94 „

The vapour density of this substance, determined by Hofmann's method in toluene vapour, gave the following results:—

	Theory. $C_3H_6O_2$	Found. I.	Found. II.
D.....	37·0	34·0	34·5

The molecular weight of acetylcarbinol was also determined by Raoult's method, using acetic acid as the solvent; the results obtained were the following:—

Substance taken	0·7660 gram.
Acetic acid	54·427 „
Depression of melting point ..	0·654°.

Molecular weight of substance found from the above data..	85
Theory for $C_3H_6O_2$.....	74

Acetylcarbinol is a colourless oil of a faint, sickly odour closely resembling that of the acetate; it boils constantly at 105—106° under a pressure of 200 mm. with very slight decomposition, and at about 147° under the ordinary pressure, but in the latter case not without decomposition, as a residue of high boiling point is always left in the retort. This residue, which probably contains condensation products of acetylcarbinol, on long standing, deposits crystals which have not yet been examined.

In a freezing mixture of powdered ice and hydrochloric acid, acetylcarbinol becomes quite thick, like glycerol, and on one occasion the substance solidified to a hard, crystalline mass.

It mixes with water, alcohol, and ether in all proportions, but is not precipitated from its aqueous solution by potassium carbonate, as is the case with solutions of acetopropyl alcohol and acetobutyl alcohol. The aqueous solution reduces ammoniacal silver solution and Fehling's solution in the cold; in the latter case the copper solution often remains unaltered for some seconds after mixing with the acetylcarbinol solution, particularly when this is weak, and then all at once reduction sets in. In some quantitative experiments it was found that 0·1 gram of acetylcarbinol dissolved in 50 c.c. of distilled water reduced about 16·5—16·6 c.c. of Fehling's solution (1 c.c. contains 0·03464 gram $CuSO_4,5Aq$ = 0·005 gram grape sugar), but it is extremely difficult to accurately detect the end point of the reaction, as the solution becomes slightly yellowish during the reduction. According to Zincke (*Ber.*, **13**, 2344), lactic acid is formed during this decomposition, thus:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH + O = CH_3{\cdot}CH(OH){\cdot}COOH;$$

and the amount of Fehling's solution reduced in the above experiments gives approximately 1 atom of oxygen to 1 mol. of acetylcarbinol.

Fehling's solution may, therefore, be used as a valuable test of the strength of aqueous acetylcarbinol solutions, and for this purpose about 2 c.c. of a weak solution (to 10 per cent.), or 1 c.c. of a stronger solution, is diluted with 50 c.c. of water, heated to about 80°, and Fehling's solution run in, as in the estimation of sugar, using, however, a flask instead of a porcelain dish, to avoid evaporation; the strength of the solution may then be roughly calculated from the data given above.

The determination of the density and magnetic rotation of acetylcarbinol was undertaken by W. H. Perkin, senr., and the following are the results of his experiments.

Density:—$d\,4°/4° = 1·0904$; $d\,15°/15° = 1·07915$; $d\,25°/25° = 1·07069$.

Magnetic Rotation.

	t.	Sp. rotation.	Mol. rotation.
	15·5°	0·9571	3·647
	„	0·9595	3·656
	„	0·9550	3·640
	„	0·9624	3·668
	„	0·9543	3·637
	„	0·9580	3·651
Average ..	15·5	0·9577	3·650

The magnetic rotation of acetylcarbinol may be calculated from that of methyl alcohol by adding the value of the acetyl group replacing hydrogen. This latter value may readily be obtained thus:—

Magnetic rotation of ethyl acetoacetate	6·501
„ „ ethyl acetate.....	4·462
Difference = Value of the acetyl group replacing hydrogen	2·039

The magnetic rotation of methyl alcohol is 1·640, and this added to 2·039 gives 3·679 as the magnetic rotation of acetylcarbinol, a number which agrees well with that actually found, namely, 3·650.

Preparation of Acetylcarbinol from Monochloracetone.

The first sample of acetylcarbinol obtained was prepared by Dr. J. B. Tingle and myself (Proc., **73**, 156) from monochloracetone by hydrolysis with water and precipitated barium carbonate; the following is an outline of the process adopted:—

25 grams of monochloracetone is slowly added from a dropping funnel to 200 c.c. of water containing an excess of freshly-precipitated barium carbonate in suspension, the whole being vigorously boiled during the operation. As soon as the monochloracetone has dissolved, and the evolution of carbonic anhydride has practically ceased, the liquid is filtered, and the resulting, almost colourless solution distilled.

The distillate is again treated with chloracetone and barium carbonate, and again distilled, the operation being repeated until 150 grams of chloracetone has been decomposed. The resulting moderately concentrated solution of acetylcarbinol is saturated with potassium carbonate, and extracted at least 50 times with pure ether. The ethereal solution is thoroughly dried over ignited potassium carbonate, and is then slowly evaporated; a colourless oil remains, the greater part of which, on distillation, passes over between 140° and 150°. On refractioning, a considerable quantity was obtained, boiling at 145—150°, which gave, on analysis, numbers agreeing with the formula $CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH$:—

0·1546 gram substance gave 0·1160 gram H_2O and 0·2766 gram CO_2.

	Theory. $C_3H_6O_2$.	Found.
C.....	48·65 per cent.	48·73 per cent.
H.....	8·10 „	8·33 „
O.....	43·24 „	42·94 „

The vapour density of this product was determined by Hofmann's method in xylene vapour, with the following results:—

	Theory. $C_3H_6O_2$.	Found. I.	Found. II.
D.....	37	35	34

The amount of acetylcarbinol obtained by this method was very small, but the yield could no doubt be much improved by concentrating the aqueous solution and isolating the ketone alcohol in the manner described on p. 792.

Action of Phenylhydrazine on Acetylcarbinol.

Acetylcarbinol Osazone, $CH_3{\cdot}C(N_2H{\cdot}C_6H_5){\cdot}CH(N_2H{\cdot}C_6H_5)$.

The phenylhydrazine compound of methylglyoxal (acetylcarbinol osazone) was first prepared by v. Pechmann (*Ber.*, **20**, 2543), by warming together aqueous solutions of methylglyoxal (or nitrosoacetone) and phenylhydrazine, thus:—

$$CH_3{\cdot}CO{\cdot}COH + 2N_2H_3{\cdot}C_6H_5 = CH_3{\cdot}C(N_2H{\cdot}C_6H_5){\cdot}CH(N_2H{\cdot}C_6H_5) + 2H_2O.$$

Subsequently, H. Laubmann (*Annalen*, **243**, 244—248) obtained the same substance by treating a solution of acetylcarbinol with phenylhydrazine. In order to prove that the substance described as acetylcarbinol in this paper really has this constitution, 5 grams of the pure substance was dissolved in 50 grams of water, a strong solution of phenylhydrazine added in excess, and the oily phenylhydrazine compound which separated digested in a sealed tube with excess of phenylhydrazine at 100—105°.

The crude osazone thus obtained, after recrystallisation from dilute alcohol, gave the following numbers on analysis:—

0·1790 gram substance gave 33·8 c.c. nitrogen; $t = 16°$; bar. = 761 mm.

	Theory. $C_{15}H_{16}N_4$.	Found.
N.....	22·22 per cent.	22·20 per cent.

This substance melted at 145°, and was identical in its properties with the compound described by v. Pechmann and H. Laubmann (*loc. cit.*).

Reduction of Acetylcarbinol.

Formation of Methylglycol, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$.

Acetylcarbinol is readily reduced by sodium amalgam with formation of methylglycol, thus:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}OH + H_2 = CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH.$$

In carrying out this experiment, a quantity of a 10 per cent. solution of acetylcarbinol was transferred to a flat porcelain dish, and treated with twice the calculated quantity of $2\frac{1}{2}$ per cent. sodium amalgam, in small portions at a time. As soon as the reduction was complete, the product was separated from the mercury, neutralised with hydrochloric acid, and slowly distilled from a flask, furnished with a long colonna, and heated by a paraffin-bath, until the residue deposited a quantity of crystals of salt. This residue was next mixed with absolute alcohol, an equal bulk of ether added, and after standing for 24 hours the solution of the glycol was separated from the precipitated salt by filtration, and evaporated; the crude oily product was then purified, first by distillation in a vacuum, and then at the ordinary pressure. In this way an almost theoretical yield of methylglycol was obtained, which boiled constantly at 188°.

The analysis gave the following results:—

0·1798 gram substance gave 0·1696 gram H_2O and 0·3132 gram CO_2.

	Theory. $C_3H_8O_2$.	Found.
C.....	47·37 per cent.	47·50 per cent.
H.....	10·53 „	10·49 „
O.....	42·10 „	42·01 „

Methylglycol was first obtained by Würtz (*Ann. Chim. Phys.* [3], **55**, 438) from propylene bromide, by digesting it with silver acetate, and subsequent hydrolysis of the acetate formed; Hartmann (*J. pr. Chem.* [2], **16**, 383) obtained the same substance in small quantity by boiling propylene bromide with an aqueous solution of sodium carbonate.

The boiling point and other properties of the substance obtained from acetylcarbinol are identical with those ascribed by Würtz to methylglycol.

The density and magnetic rotations of methylglycol were determined by W. H. Perkin, sen.

Density:—$d\,4°/4° = 1·0464$; $d\,15°/15° = 1·0389$; $d\,25°/25° = 1·03367$.

Magnetic Rotation.

	t.	Sp. rotation.	Mol. rotation.
	15·5°	1·0058	4·098
	„	1·0061	4·099
	„	1·0055	4·096
	„	1·0018	4·082
	„	1·0042	4·091
Average ..	15·5	1·0047	4·093

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, July*, 1889. Vol. LV.]

ACETOPROPYL ALCOHOL AND ACETOBUTYL ALCOHOL.

By Harold G. Colman, M.Sc., Ph.D., and W. H. Perkin, Junr.

In a previous communication to the Society (Trans., 1887, **51**, 702), it was shown by one of us that acetobutyl alcohol, obtained by boiling methyldehydrohexonecarboxylic acid with water, differs very widely from the substance of that name obtained by Lipp (*Ber.*, 1885, 3280) by boiling ethylic ω-bromopropylacetoacetate with dilute hydrochloric acid, the boiling point of the former being 227°, whereas the latter product distilled at 154—155°, a difference of 70°.

In a paper published some time since (*Ber.*, 1888, 2138), "On the Action of Sodium on Ethylic Monochloracetate," Fittig and Erlenbach, in describing a substance boiling at 128°, which they supposed to be acetoisopropyl alcohol, took occasion to state that the acetobutyl and acetopropyl alcohols previously described by us could not possibly have the constitution assigned to them—owing to their syrupy consistency and high boiling points—and that the description given by Lipp of his acetobutyl alcohol agreed much better with the properties such a substance might be expected to possess. In a later paper (*Ber.*, 1888, 2647), these chemists discovered that their compound was not acetoisopropyl alcohol, but was simply acetol ethyl ether, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}O{\cdot}C_2H_5$.

As, however, in spite of this, they did not withdraw their previous remarks on the nature of acetopropyl and acetobutyl alcohols, and as we have extensively used these substances in the synthesis of ring-derivatives, and drawn important theoretical conclusions from the results obtained, we have thought it necessary to again carefully examine these alcohols with a view to further establishing their identity.

If the question of the probable properties of such a substance as acetobutyl alcohol, $CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2{\cdot}OH$, is carefully examined, it is soon apparent that a compound of this formula should be a thick oil boiling considerably above 200°.

Taking into account a large number of cases, it is found that the usual result of displacing one hydrogen-atom in an organic substance (boiling between 100° and 130°) by the group $CH_3{\cdot}CO$, is to raise the boiling point of that substance some 100° to 120°.

Now, taking normal butyl alcohol (b. p. 118°) as a basis, and substituting $CH_3{\cdot}CO$ for one hydrogen-atom, we find that the calculated boiling point of acetobutyl alcohol lies between 218° and 238°, whilst the boiling point observed was 227°. Again, acetobutyl alco-

hol would, in its physical properties, bear considerable resemblance to the class of glycols, and this is borne out by the fact that these compounds, and particularly the higher numbers, are thick, oily liquids boiling at high temperatures.

In the original investigation of acetobutyl alcohol (Trans., 1887, **51**, 717—725) the following attempts were made to prove its constitution.

The ketonic nature of the substance was demonstrated by the fact that it combined with phenylhydrazine—the fact that it was also an alcohol was shown by its being converted into acetobutyl bromide on treatment with aqueous hydrobromic acid. The portion of the carbonyl-group in relation to the alcohol-group was shown by the behaviour of acetobutyl alcohol on oxidation, when it decomposed first into acetobutyric acid and then, under the influence of an excess of oxidising agent, into acetic acid and succinic acid:—

(1.) $CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2{\cdot}OH + O_2 = CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}COOH + H_2O.$

(2.) $CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2{\cdot}OH + 5O = CH_3{\cdot}COOH + COOH{\cdot}CH_2{\cdot}CH_2{\cdot}COOH + H_2O.$

The constitution of acetobutyl alcohol is also clearly demonstrated by the reduction of acetobutyl bromide to methyl butyl ketone by means of zinc and acetic acid:—

$$CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_2Br + H = CH_3{\cdot}CO{\cdot}[CH_2]_3{\cdot}CH_3 + HBr.$$

The constitution of acetopropyl alcohol was proved by the fact that this substance on oxidation yields levulinic acid, thus:—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH + O_2 = CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}COOH + H_2O.$$

Fittig, however, does not consider this a proof of the constitution of this alcohol (*Ber.*, **21**, 2139).

In order, if possible, to bring further proof of the constitution of these two important ketone alcohols, specimens of each were prepared and purified with the greatest care, and their magnetic rotation determined by Dr. W. H. Perkin, senr. The numbers obtained showed clearly that these substances had the constitution assigned to them, and that they were two members of a homologous series, the difference for CH_2 being found as 0·958 instead of 1·023.

These proofs of the constitution of the acetopropyl and acetobutyl alcohols being so satisfactory, all that remained to be done was to examine into the nature of the substance described by Lipp as acetobutyl alcohol, and to determine in what respects this substance differed from the acetobutyl alcohol obtained by boiling methyldehydrohexanecarboxylic acid with water.

The hydrolysis of ethylic ω-propylacetoacetate by means of hydrochloric acid was therefore carried out according to Lipp's directions, and as a result an oil was obtained which, on analysis, gave numbers agreeing approximately with those required for acetobutyl alcohol, and which distilled apparently at 154—155°. Subsequent experiments showed, however, that this temperature, instead of being the boiling point, was in reality the decomposing point of the alcohol: the reason for this being, that the slightest trace of impurity is sufficient to prevent acetobutyl alcohol from distilling without the most rapid decomposition into its anhydride (methyldehydrohexone) and water, the thermometer remaining constant at 154—155°.

Lipp's acetobutyl alcohol, when not too impure, can be distilled with slight decomposition under reduced pressure; the boiling point noticed in two cases being 157° under 100 mm. pressure and 171° under 177 mm. pressure; on distilling acetobutyl alcohol from methyldehydrohexonecarboxylic acid under the same conditions, almost identical boiling points were noticed.

Pure acetobutyl alcohol was obtained from Lipp's crude product by distilling with steam, fractioning the methyldehydrohexone thus obtained, and treating it with water. In this way a thick oil was obtained which distilled under ordinary pressure at 225—227°, and was in every respect identical with the acetobutyl alcohol from methyldehydrohexonecarboxylic acid.

These and other experiments, an account of which will be given later on, prove conclusively that acetobutyl alcohol when pure boils at 225—227°, and not at 154—155° as stated by Lipp. Acetopropyl alcohol behaves in every respect, physically as well as chemically, as the lower homologue of acetobutyl alcohol, and as this substance gives levulinic acid on oxidation, no further experiments in proof of its constitution are necessary.

Preparation of Acetobutyl Alcohol by Lipp's Method.

In repeating Lipp's experiments, his instructions, as given in the *Berichte*, **18**, 3275, were followed exactly, with the one exception that instead of 80 grams of trimethylene bromide 50 only were taken, the former number being evidently a misprint, as is clearly seen from the fact that Lipp mentions that he uses 1 mol. of trimethylene bromide to 1 mol. of ethylic sodacetoacetate.

The oil obtained by the addition of water to the product of the reaction was washed with caustic potash solution, and then with water, and dried over potassic carbonate. This crude ethylic bromopropyl acetoacetate weighed from 55 to 60 grams; it contained as impurity considerable quantities of trimethylene bromide and some

ethyl methyldehydrohexonecarboxylate, besides small quantities of ethylic acetoacetate. This oil was now digested with hydrochloric acid, the same quantities being used as given by Lipp, the product separated from the unchanged trimethylene bromide (about 20 grams), and about one-fifth of the water distilled off. The solution was then saturated with potassic carbonate, and the oily layer which separated dried over potassic carbonate, and allowed to stand for three or four days over sulphuric acid in a vacuum as Lipp directs, and then analysed.

Two different samples gave the following numbers:—

I. 0·1545 gram substance gave 0·1390 gram H_2O and 0·3380 gram CO_2.

II. 0·2340 gram substance gave 0·2090 gram H_2O and 0·5150 gram CO_2.

	Calculated for $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$.	Found. I.	Found. II.
C	62·06 p. c.	59 67	60·02 p. c.
H	10·35 „	10·00	9·92 „
O	27·59 „	30·33	30·06 „

An examination of this oil showed that it contained, besides other impurities, small quantities of bromine. On submitting it to fractional distillation under the ordinary pressure, the thermometer rises rapidly to 150°, at which temperature vigorous decomposition sets in, and between 150—160° almost the whole distils over, the distillate consisting of two layers, the upper one being a mixture of methyldehydrohexone with acetobutyl alcohol, and the lower one acetobutyl alcohol and water. The boiling point, 154—155° (718 mm.), given by Lipp is, therefore, evidently the decomposition point of this crude alcohol into water and its anhydride methyldehydrohexone. These recombine to some extent in the receiver, and probably almost entirely on standing.

A very carefully prepared sample of Lipp's product was now fractioned under reduced pressure (100 mm.), when it was found to boil fairly constantly at 157° with very little decomposition. An analysis of this preparation gave the following result:—

0·1335 gram substance gave 0·1260 gram H_2O and 0·3015 gram CO_2.

	Calculated for $C_6H_{12}O_2$.	Found.
C	62·06 per cent.	61·59 per cent.
H	10·35 „	10·49 „
O	27·59 „	27·92 „

Even after distillation in a vacuum, this alcohol is far from pure, and attempts to refraction the product invariably lead to its decomposing into anhydride and water even under very low pressures such as 20—30 mm., and, curiously enough, although this substance was prepared a great number of times, it was only on two occasions found posssible to distil it at all.

An attempt was next made to purify this crude substance by distillation in a current of steam. About 30 grams of the crude oil were taken, and the distillate containing a quantity of oil in suspension was extracted with ether. The ethereal solution was dried carefully over carbonate of potash, the ether distilled off, and the resulting oil distilled. Almost the whole passed over between 105° and 111°, and on re-fractioning a beautifully colourless oil was obtained boiling constantly at 109°, and consisting of pure methyldehydrohexone, as the following analysis shows:—

0·2100 gram substance gave 0·1947 gram H_2O and 0·5638 gram CO_2.

	Calculated for $C_6H_{10}O$.	Found.
C	73·46 per cent.	73·21 per cent.
H	10·20 „	10·29 „
O	16·33 „	16·50 „

When shaken with a considerable quantity of distilled water and allowed to stand for some days, this oil completely dissolves forming acetobutyl alcohol. On saturating the solution with carbonate of potash, extracting with ether, drying very thoroughly over carbonate of potash, and evaporating, a colourless oil was obtained which under the ordinary pressure distilled without decomposition between 225—227°, and gave the following numbers on analysis, showing that it was pure acetobutyl alcohol.

0·1604 gram substance gave 0·1538 gram H_2O and 0·3657 gram CO_2.

	Calculated for $C_6H_{12}O_2$.	Found.
C	62·06 per cent.	62·17 per cent.
H	10·35 „	10·65 „
O	27·59 „	27·18 „

On careful examination, this substance was found to be identical in all respects with the acetobutyl alcohol previously obtained by one of us (Trans., **51**, 716—720) by boiling methyldehydrohexonecarboxylic acid with water—

$$\begin{matrix} CH_3\cdot C\cdot O-CH_2 \\ \| \quad\quad | \\ COOH\cdot C\cdot CH_2\cdot CH_2 \end{matrix} + H_2O = \begin{matrix} CH_3\cdot CO \\ | \\ CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH \end{matrix} + CO_2.$$

The decomposition represented by this equation is not only a quantitative one, but the acetobutyl alcohol obtained is so pure that when perfectly dry it distils at once at 227° with the merest trace of decomposition, the resulting product being almost free from smell.

The camphoric odour which Lipp ascribes to his product is due to various impurities, and particularly to methyldehydrohexone, the presence of this substance would also explain the mobility of Lipp's alcohol.

Acetopropyl Alcohol, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, *and Acetopropyl Bromide*, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$.

The acetopropyl alcohol used in the following experiments was prepared according to a method previously described (Trans., 1887, **51**, 829), which consists in boiling acetyltrimethylenecarboxylic acid with water until the evolution of carbon dioxide ceased, saturating the liquid with potassic carbonate, and extracting with ether. The product obtained boiled constantly at 144—145° (100 mm.), and possessed all the properties previously assigned to it.

To prepare acetopropyl bromide, the alcohol was mixed with a saturated aqueous solution of hydrogen bromide, and the liquid heated on a water-bath for one hour. The product was poured into water, the excess of hydrogen bromide neutralised with sodic carbonate, and the bromide repeatedly extracted with ether, the ethereal solution evaporated, and the resulting oil fractioned under a pressure of 90 mm. Almost the whole of it distilled at 115—120°, a little hydrogen bromide being eliminated, as is also the case in the distillation of acetobutyl bromide; owing to this decomposition, the bromine determinations made with a product boiling constantly at 118° (90 mm.) came a little too low.

I. 0·1548 gram substance gave 0·1687 gram AgBr.

II. 0·1807 gram substance gave 0·1973 gram AgBr.

III. 0·2350 gram substance gave 0·2480 gram AgBr and 0·0050 gram Ag.

	Calculated for $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br$.	Found. I.	II.	III.
Br	48·48 p. c.	46·37	46·42	46·48 p. c.

When freshly distilled, acetopropyl bromide is a colourless mobile liquid, which has a penetrating odour closely resembling that of acetobutyl bromide. On standing, it rapidly becomes dark coloured, especially when acted on by light.

Acetopropyl bromide is remarkable for the ease with which it decomposes with elimination of hydrogen bromide. Experiments

made on the action of sodic ethylate and ethylic sodiomalonate on this bromide invariably resulted in the formation of a light, ethereal oil boiling at 113°, which appears to be identical with acetyltrimethylene (Trans., 1887, **51**, 832). In that case, it would seem that the elimination of hydrogen bromide took place according to the equation—

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br = CH_3{\cdot}CO{\cdot}CH\begin{matrix}\diagup\\ \\ \diagdown\end{matrix}\begin{matrix}CH_2\\ \\ CH_2\end{matrix}>CH_2 + HBr.$$

As we were on the point of forwarding this paper for publication, we received the last number of the *Berichte*, containing an article by Lipp on acetopropyl alcohol (*Ber.*, **22**, 1196).

In this article Lipp describes a repetition of the experiments made some time since by Freer and Perkin (Trans., 1887, **51**, 834—835) on the action of hydrogen chloride on ethylic ω-bromethylacetoacetate, his results confirming in every particular those previously obtained. On account of the comparatively high temperature at which acetopropyl alcohol boils, Lipp states in a footnote (p. 1198) that the boiling point of acetobutyl alcohol previously given by him, is probably the decomposition point of this substance, a view which agrees with that deduced by us from the results of the experiments described in our present paper. Lipp then proceeds to describe the preparation of acetopropyl alcohol by the hydrolysis of the crude product of the action of ethylene bromide on ethylic sodacetoacetate (ethylic ω-bromethylacetoacetate), and gives in detail the conversion of this alcohol into levulinic acid by oxidation. These reactions have already been carefully studied by Freer and Perkin (Trans., 1887, **51**, 834) and by Colman and Perkin (1888, **53**, 189—190). Lipp also prepared ω-bromopropyl methyl ketone (acetopropyl bromide) by treating acetopropyl alcohol with hydrogen bromide, and his description of this substance agrees in every respect with that given by us in this paper.

In this interesting paper on acetobutyl alcohol, Lipp has unfortunately based his criticisms of the results previously obtained by us on short and very incomplete abstracts of our papers which have from time to time appeared in the *Chemisches Centralblatt*, and he has thus been led to make a number of experiments which otherwise would have been unnecessary.

To this cause is also to be attributed the statement that he makes that we never prepared acetopropylalcohol in a pure condition, and that we obtained it only as a very thick, unstable oil, which decomposed on distillation. On referring to our original papers (*loc. cit.*), it will be found that every pains was taken to get this substance in an especially pure condition, in order to allow of its magnetic rotation being deter-

mined, and, as a result, a beautiful product was obtained, boiling constantly at 144—145° (100 mm. pressure), and this, as the analytical numbers, as well as those obtained in the determination of its magnetic rotation show, must have been very pure indeed. Both acetopropyl alcohol and acetobutyl alcohol have been prepared by us in very large quantities for use in various synthetical experiments, and experience has shown that these substances are very readily obtained in a state of purity by boiling acetyltrimethylene- and methyldehydrohexone-carboxylic acids with water, whereas the products obtained by the hydrolysis of ethylic ω-bromethyl- and bromopropyl-acetoacetates are invariably very crude and difficult to purify. A criticism of the remarks which Lipp makes, at the conclusion of his article, as to the constitution of ethylic acetyltrimethylene carboxylate, will form the subject of a future paper.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Benzoylacetic Acid and some of its Derivatives. Part V.

By W. H. Perkin, Jun., Ph.D., F.R.S., and James Stenhouse.

In previous investigations on ethyl benzoylacetate (Trans., 1884, **45**, 170; 1885, **47**, 240, 262; 1886, **49**, 154), it was shown that in its general behaviour it bore a very strong resemblance to ethyl acetoacetate. When treated with sodium ethylate, it forms a well-characterised sodium compound, $C_6H_5{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5$, which, by the action of alkyl haloïds, yields monalkyl substitution products. It still remained to be seen whether these alkyl derivatives, like the monosubstituted derivatives of ethyl acetoacetate, if again treated with sodium ethylate and alkyl haloïds, were capable of forming di-substitution products.

Numerous experiments were made on this subject, and, as a result, it was found that the mono-substituted ethyl benzoylacetates, such as ethyl methylbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}CH(CH_3){\cdot}COOC_2H_5$, when treated in the usual way in alcoholic solution with sodium ethylate and isobutyl iodide or benzyl chloride, were only to a small extent converted into di-substitution products, the bulk of the substance being hydrolysed by the sodium ethylate employed, with formation of benzoic and fatty acids, and, in the case of the benzyl chloride, a quantity of benzyl ethyl ether, $C_6H_5{\cdot}CH_2{\cdot}OC_2H_5$, was obtained.

Allyl iodide, on the other hand, converts the sodium compound of ethyl methylbenzoylacetate almost quantitatively into ethyl methylallylbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}C(CH_3)(CH_2{\cdot}CH{:}CH_2){\cdot}COOC_2H_5$, and it is difficult to understand why allyl iodide should behave so differently from isobutyl iodide, unless indeed the former is more readily decomposed than the latter.

That the mono-substituted derivatives of ethyl benzoylacetate are capable of forming sodium compounds is clearly shown by the fact that the ethereal solutions of these compounds dissolve sodium with evolution of hydrogen. The resulting ethereal solutions of the sodium compounds react only very slowly with alkyl haloïds, although, on the addition of an acid chloride, separation of sodium chloride at once takes place.

Thus, the sodium compound of ethyl methylbenzoylacetate is readily acted on by benzoyl chloride with formation of ethyl methyldibenzoylacetate:—

$$C_6H_5\cdot CO\cdot CNa(CH_3)\cdot COOC_2H_5 + C_6H_5\cdot COCl = (C_6H_5\cdot CO)_2C(CH_3)\cdot COOC_2H_5 + NaCl.$$

The conclusion which may be drawn from these experiments is that ethyl benzoylacetate differs from ethyl acetoacetate in this respect, that, unlike the latter, it only with difficulty yields di-substitution products; it is, however, possible that under conditions other than those employed in this investigation, these di-substituted products may be more readily obtained, and experiments on this point are in progress.

The substance described in a previous paper (Trans., 1884, **45**, 181) as ethyl diethylbenzoylacetate, $C_6H_5\cdot CO\cdot C(C_2H_5)_2\cdot COOC_2H_5$, is very probably a mixture of this substance with considerable quantities of ethyl ethylbenzoylacetate, $C_6H_5\cdot CO\cdot CH(C_2H_5)\cdot COOC_2H_5$, a supposition which is borne out by the analytical numbers obtained in a subsequent examination of this product.

In the course of this investigation, we have taken the opportunity of correcting some errors which had crept into the previous work on the subject; we have also prepared a number of new and interesting compounds, and, before entering into experimental details, it will be well to give a brief account of the results obtained.

When the sodium compound of ethyl benzoylacetate is treated in ethereal solution with benzoyl chloride, ethyl dibenzoylacetate is produced:—

$$C_6H_5\cdot CO\cdot CHNa\cdot COOC_2H_5 + C_6H_5\cdot COCl = (C_6H_5\cdot CO)_2CH\cdot COOC_2H_5 + NaCl.$$

This interesting compound, which was previously described as an oil, is crystalline, and melts at 112°; on hydrolysis, it yields the corresponding dibenzoylacetic acid without decomposition.

Ethyl methyldibenzoylacetate, $(C_6H_5\cdot CO)_2C(CH_3)\cdot COOC_2H_5$ (see above), is, on the other hand, much less stable than ethyl dibenzoylacetate, as, when treated with alkalis, it is decomposed with formation of benzoic acid.

As dibenzoylacetic acid contains two carbonyl groups, it was thought probable that, when treated with hydroxylamine, it would yield a di-oxime, $[C_6H_5\cdot C(NOH)]_2CH\cdot COOH$; on making the experiment in alkaline solution, a substance, $C_9H_7NO_2$, was obtained, which, on examination, was found to be identical with *phenylisoxazolone*, $C_6H_5\cdot\overset{\overset{\displaystyle N}{\|}}{C}\cdot CH_2\cdot\overset{\overset{\displaystyle O}{|}}{CO}$, which L. Claisen and W. Zedel (*Ber.*, **24**, 140) prepared by treating ethyl benzoylacetate with hydroxylamine in acetic acid solution. Under these circumstances, dibenzoylacetic acid is obviously decomposed with formation of benzoic and benzoyl-

acetic acids, the latter then combining with hydroxylamine to form phenylisoxazolone.

In like manner, ethyl dibenzoylacetate and ethyl dibenzoylmethylacetate, when heated with phenylhydrazine, are decomposed with formation of benzoylphenylhydrazine, $C_6H_5{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}C_6H_5$.

Dibenzoylacetic acid is readily reduced by sodium amalgam in alkaline solution with formation of dihydroxydibenzylacetic acid, $[C_6H_5{\cdot}CH(OH)]_2CH{\cdot}COOH$; but, at the same time, considerable quantities of β-phenyllactic acid, $C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}COOH$, are produced, showing that a portion of the dibenzoylacetic acid, during the operation, had been decomposed into benzoylacetic and benzoic acids.

Ethyl ethylbenzoylacetate, when treated with sodium amalgam, yields α-ethyl-β-phenylhydroxypropionic acid,

$$C_6H_5{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH$$

(m. p. 106—108°).

α-Methyl-β-phenylhydroxypropionic acid, when heated at a high temperature, is decomposed with formation of water, carbonic anhydride, and allylbenzene (methylstyrolene), $C_6H_5{\cdot}CH{:}CH{\cdot}CH_3$.

Furfuraldehyde readily condenses with *ethyl benzoylacetate*, when a mixture of the two is digested with acetic anhydride, yielding ethyl furfuralbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}C(:CH{\cdot}C_4H_3O){\cdot}COOC_2H_5$, which melts at 68°.

Ethyl nitrosobenzoylacetate dissolves readily in potassium hydrate solution, and, on standing, is gradually decomposed with formation of nitrosoacetophenone, $C_6H_5{\cdot}CO{\cdot}CH{:}NOH$, benzoic acid, and other products.

Ethyl benzylbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}CH(C_7H_7){\cdot}COOC_2H_5$ (b. p. 265°, 80 mm.), is readily produced when the sodium compound of ethyl benzoylacetate is digested in alcoholic solution with benzyl chloride.

On hydrolysis, this ethereal salt is decomposed with formation of benzylacetophenone, $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}C_6H_5$, a crystalline substance which melts at 70° and, on treatment with hydroxylamine, yields an oxime, $C_6H_5{\cdot}C(NOH){\cdot}CH_2{\cdot}CH_2{\cdot}C_6H_5$, melting at 80—81°.

Reduction with sodium, in moist ethereal solution, converts benzylacetophenone into diphenyl propyl alcohol,

$$C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_2{\cdot}C_6H_5,$$

a thick, colourless oil which boils at 240° (70 mm.).

Experiments on the Formation of Di-substitution Derivatives of Ethyl Benzoylacetate.

Exp. I.—Ethyl methylbenzoylacetate (1 mol.) was digested in alcoholic solution with sodium ethylate (1 mol.) and excess of isobutyl

iodide at 100° for two hours. The product was heated on a water-bath till free from alcohol, mixed with water, extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the residual oil fractioned under reduced pressure. The greater part of the oil passed over between 160° and 170°, under a pressure of 225 mm., only a small quantity of an oil of high boiling point remaining in the retort.

On distillation under ordinary pressures, about three-quarters of the fraction 160—170° (225 mm.) passed over between 210—211°, and the distillate was found, on analysis, to consist of slightly impure ethyl benzoate.

0·1116 gram substance gave 0·0728 gram H_2O and 0·2950 gram CO_2.

	Theory. $C_6H_5\cdot COOC_2H_5$.	Found.
C	72·00 per cent.	72·92 per cent.
H	6·66 „	7·24 „
O	21·33 „	19·84 „

This crude ethereal salt gave, on hydrolysis, almost pure benzoic acid, which, after recrystallisation from water, melted at 120°.

Exp. II.—Ethyl methylbenzoylacetate (1 mol.) was digested in alcoholic solution with sodium ethylate (1 mol.) and excess of benzyl chloride. The product, isolated as above, was first distilled under reduced pressure and then fractioned under the ordinary pressure. Almost the whole passed over between 175° and 200°, leaving only a small residue, of a high boiling point, in the retort. On refractioning the oil boiling at 175—200°, a considerable quantity of a colourless distillate was obtained, boiling constantly at 185°; this, on examination, was found to consist of benzyl ethyl ether, $C_6H_5\cdot CH_2\cdot OC_2H_5$.

These and other experiments were repeated under various conditions, but in all cases the results were similar, except in the case of allyl iodide, which gives with the sodium compound of ethyl methylbenzoylacetate a very good yield of ethyl allylmethylbenzoylacetate (see next section).

Ethyl Allylmethylbenzoylacetate,
$C_6H_5\cdot CO\cdot C(CH_2\cdot CH{:}CH_2)(CH_3)\cdot COOC_2H_5$.

In order to prepare this ethereal salt, ethyl methylbenzoylacetate (1 mol.) was mixed with an alcoholic solution of sodium ethylate (1 mol.), an excess of allyl iodide added, and the whole heated on a water-bath for three hours in a flask connected with a reflux apparatus. After distilling off the alcohol, water was added, the product extracted twice with ether, the ethereal solution washed with water and a

little sulphurous acid, dried over calcium chloride, evaporated, and the residual oil purified by repeated fractionation under reduced pressure (225 mm.). In this way a considerable quantity of a colourless oil was obtained, boiling at 243—245°, which, on analysis, gave the following numbers :—

0·1032 gram substance gave 0·0681 gram H_2O and 0·2774 gram CO_2.

	Theory. $C_{15}H_{18}O_3$.	Found.
C	73·17 per cent.	73·25 per cent.
H	7·32 „	7·36 „
O	19·51 „	19·39 „

Ethyl allylmethylbenzoylacetate is readily hydrolysed by boiling with alcoholic potassium hydrate solution ; the principal products of the reaction are benzoic acid and an oily fatty acid of disagreeable odour, probably allylmethylacetic acid. A small quantity of a neutral substance is also formed, which boils approximately at 235° ; this is presumably methylallylacetophenone, but it was not further examined.

Ethyl Dibenzoylacetate, $[C_6H_5{\cdot}CO]_2CH{\cdot}COOC_2H_5$.

The sodium compound of ethyl benzoylacetate reacts readily with benzoyl chloride with formation of ethyl dibenzoylacetate, thus :—

$$C_6H_5{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_6H_5{\cdot}COCl = (C_6H_5{\cdot}CO)_2CH{\cdot}COOC_2H + NaCl.$$

This ethereal salt can only be obtained in a crystalline condition if the ethyl benzoylacetate employed is very pure and free from acetophenone, and to the presence of the latter in considerable quantity in the ethyl benzoylacetate prepared from phenylpropiolic acid is due the fact that this substance was previously only obtained as an oil (Trans., 1885, **47**, 246).

In preparing large quantities of ethyl dibenzoylacetate, we have found the following method to give good results :—

25 grams of ethyl benzoylacetate is dissolved in 250 grams of pure dry ether, 3 grams of sodium, in the form of fine wire, added, and the whole allowed to stand until the sodium has completely dissolved, care being taken that the temperature does not rise above 25°. 19 grams of freshly distilled benzoyl chloride is then added slowly through a dropping funnel, the mixture allowed to stand for two hours, diluted with water, the ethereal solution separated, washed with water, and allowed to stand for 24 hours in a cool place. The crystalline mass which separates is collected, washed with ether, and dried on a porous plate over sulphuric acid under diminished

pressure. The beautifully crystalline, colourless powder thus obtained consists of pure ethyl dibenzoylacetate, as the following analyses show :—

0·1478 gram substance gave 0·0741 gram H_2O and 0·3970 gram CO_2.

0·1626 gram substance gave 0·0815 gram H_2O and 0·4351 gram CO_2.

	Theory. $C_{18}H_{16}O_4$.	Found. I.	II.
C	72·97 per cent.	73·25	72·97 per cent.
H	5·41 „	5·57	5·57 „
O.	21·62 „	21·18	21·46 „

Ethyl dibenzoylacetate melts at 112°. It is sparingly soluble in ether, readily soluble in boiling alcohol, insoluble in water.

The ethereal mother liquors from the pure crystalline compound, on evaporation, deposit a yellow oil, which solidifies to a great extent on long standing over sulphuric acid in a vacuum. The crude pasty product thus obtained may be readily purified by contact with a porous plate until free from oily impurity, and subsequent trituration with absolute ether.

Ethyl dibenzoylacetate is readily hydrolysed by boiling with alcoholic potassium hydrate, with formation of dibenzoylacetic acid; the details of this operation, and the method of purification of the resulting acid, have been already given (Trans., 1885, **47**, 246).

Reduction of Dibenzoylacetic Acid. Formation of Dihydroxydibenzylacetic Acid, $[C_6H_5{\cdot}CH(OH)]_2CH{\cdot}COOH$, *and β-Phenyllactic Acid*, $C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}COOH$.

Dibenzoylacetic acid is readily reduced by sodium amalgam in alkaline solution with formation of a mixture of dihydroxydibenzylacetic acid and β-phenyllactic acid.

The former acid is produced by the direct reduction of dibenzoylacetic acid, thus :—

$$(C_6H_5{\cdot}CO)_2CH{\cdot}COOH + 2H_2 = [C_6H_5{\cdot}CH(OH)]_2CH{\cdot}COOH.$$

The latter acid results obviously from the reduction of benzoylacetic acid, which is produced by the decomposition of dibenzoylacetic acid in the presence of alkali, thus :—

$$(C_6H_5{\cdot}CO)_2CH{\cdot}COOH + H_2O = C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}COOH + C_6H_5{\cdot}COOH.$$

$$C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}COOH + H_2 = C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}COOH.$$

Pure dibenzoylacetic acid was dissolved in a warm dilute solution of sodium carbonate, well cooled, and treated with a considerable excess of $2\frac{1}{2}$ per cent. sodium amalgam in small quantities at a time. As the reduction proceeds, the solution becomes slightly turbid and smells of acetophenone, a small quantity of a dark-coloured sticky substance separates, which, however, owing to the small amount of material at our disposal, could not be obtained in a pure condition. The formation of a similar neutral reduction product was observed in experimenting on the action of sodium amalgam on ethyl benzoylacetate (Trans., 1885, **47**, 255); this was ultimately purified, and obtained in the form of colourless prisms melting at 102°; it seems very possible that this same substance is formed in both experiments, especially as the sticky substance from the reduction of dibenzoylacetic acid gives with alcoholic potash the intense magenta-red coloration, which is characteristic of the compound melting at 102°.

In order to isolate the principal products of the reduction of dibenzoylacetic acid, the alkaline solution was separated from the mercury by means of a separating funnel, acidified with dilute sulphuric acid, extracted several times with ether, and the ethereal solution dried over calcium chloride and evaporated. The yellowish oil thus obtained was digested with an excess of boiling baryta water for a short time, the excess of baryta removed by passing a rapid current of carbonic anhydride, the liquid filtered, and the colourless filtrate extracted twice with ether. In this way a small quantity of a neutral substance is removed; this will be referred to again later on.

The aqueous solution was then acidified with hydrochloric acid, extracted four times with ether, the ethereal solution dried over calcium chloride, evaporated, and the thick, almost colourless, oily residue allowed to stand over sulphuric acid under diminished pressure for several days. In order to remove the oily impurities, the resulting semi-solid mass was stirred up with successive small quantities of benzene, when a crystalline residue was left, which became quite colourless after repeated washing with benzene on a filter pump.

The crystals were then dissolved in a little hot water, the solution filtered, and allowed to cool slowly, and in this way beautiful, transparent, colourless needles were obtained, which after drying over sulphuric acid under diminished pressure, gave the following numbers on analysis :—

0·1526 gram substance gave 0·0808 gram H_2O and 0·3926 gram CO_2.

0·1586 gram substance gave 0·0848 gram H_2O and 0·4080 gram CO_2.

	Theory. $[C_6H_5\cdot CH(OH)]_2CH\cdot COOH$.	Found. I.	Found. II.
C	70·59 per cent.	70·16	70·16 per cent.
H	5·88 „	5·89	5·94 „
O	23·53 „	23·95	23·90 „

Dihydroxydibenzylacetic acid melts at 188—190°, but not very sharply. It is readily soluble in hot water and alcohol, sparingly so in benzene and light petroleum.

The dissociation constant for the electrical conductivity of dihydroxydibenzylacetic acid at different concentrations was determined by Dr. Walker, who found K = 0·0051.

The basicity of this acid was determined by titration with a standard solution of potassium hydrate (1 c.c. = 0·00559 gram KOH).

0·1552 gram of the pure acid required for neutralisation 5·8 c.c. of the potassium hydrate solution = 0·0324 gram KOH.

A monobasic acid of the formula $C_{16}H_{16}O_4$ requires 0·0319 gram KOH.

The dilute solution of the potassium salt shows the following behaviour with reagents:—*Copper acetate*, a light-green precipitate, very sparingly soluble in water; *lead acetate*, a white, caseous precipitate, insoluble in water; *barium chloride*, no precipitate; *zinc acetate*, no precipitate.

On spontaneous evaporation, the benzene mother liquors from the above acid gradually deposit needle-shaped crystals; these were collected, washed with a little benzene, recrystallised from this solvent, and analysed with the following result:—

0·1501 gram substance gave 0·0812 gram H_2O and 0·3586 gram CO_2.

	Theory. $C_6H_5\cdot CH(OH)\cdot CH_2\cdot COOH$.	Found.
C	65·06 per cent.	65·16 per cent.
H	6·03 „	6·01 „
O	28·91 „	28·83 „

This substance melts at 91—93°, and is identical with the β-phenyllactic acid obtained by the reduction of benzoylacetic acid with sodium amalgam.

The silver salt was prepared by precipitating a neutral solution of the ammonium salt by silver nitrate. It gave the following results on analysis:—

0·2262 gram substance gave on ignition 0·0898 gram Ag = 39·61 per cent. Theory, $C_6H_5\cdot CH(OH)\cdot CH_2COO$, Ag = 39·56 per cent.

The neutral oily substance obtained in the purification of the crude product of the action of sodium amalgam on dibenzoylacetic acid as described above solidified, almost completely, on standing. The crude product was spread on a porous plate and allowed to stand until the traces of oily impurity were entirely absorbed, and the colourless crystals analysed with the following result:—

0·0508 gram substance gave 0·0322 gram H_2O and 0·1478 gram CO_2.

	Theory. $C_{15}H_{16}O_2$.	Found.
C.....	78·95 per cent.	79·33 per cent.
H.....	7·01 „	7·04 „
O.....	14·04 „	13·63 „

This substance, which melts at about 129°, is probably diphenyltrimethyleneglycol, $C_6H_5{\cdot}CH(OH){\cdot}CH_2{\cdot}CH(OH){\cdot}C_6H_5$, produced by the reduction of dibenzoylmethane, $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}C_6H_5$, which is one of the decomposition products of dibenzoylacetic acid.

Action of Hydroxylamine on Dibenzoylacetic Acid, and of Phenylhydrazine on Ethyl Dibenzoylacetate.

As dibenzoylacetic acid is a moderately stable substance, it seemed probable that, when treated with hydroxylamine in alkaline solution, it would yield a dioxime of the formula $[C_6H_5{\cdot}C(NOH)]_2CH{\cdot}COOH$, the examination of which might lead to very interesting results.

With the object of preparing this compound, pure dibenzoylacetic acid (1 mol.) was dissolved in methyl alcohol, mixed with a concentrated aqueous solution of hydroxylamine hydrochloride (3 mols.), an excess of potassium hydrate (6 mols.) added, and the whole allowed to stand for two days. The product was evaporated at a low temperature until free from methyl alcohol, mixed with water, acidified with dilute hydrochloric acid, and the crystalline precipitate which separated collected, washed with water, dried on a porous plate, and recrystallised twice from methyl alcohol. The beautiful crystalline compound thus obtained gave, on analysis, the following numbers:—

0·1320 gram substance gave 0·0586 gram H_2O and 0·3266 gram CO_2.

0·1648 gram substance gave 12·4 c.c. nitrogen; $t = 16°$; bar. = 732 mm.

	Theory. $C_9H_7NO_2$.	Found.
C.....	67·08 per cent.	67·47 per cent.
H.....	4·35 „	4·93 „
N.....	8·69 „	8·44

This substance melts at 146° with decomposition, and is identical with the phenylisoxazolon which L. Claisen and W. Zedel (*Ber.*, **24** 140) obtained by treating ethyl benzoylacetate in acetic acid solution with hydroxylamine, thus:—

$$C_6H_5\cdot CO\cdot CH_2\cdot COOC_2H_5 + NH_2\cdot OH = \begin{matrix} C_6H_5\cdot C\cdot CH_2\cdot COOC_2H_5 \\ \| \\ N\cdot OH \end{matrix} + H_2O.$$

$$\begin{matrix} C_6H_5\cdot C\cdot CH_2\cdot COOC_2H_5 \\ \| \\ N\cdot OH \end{matrix} = \begin{matrix} C_6H_5\cdot C\cdot CH_2\cdot CO \\ \| \quad\quad | \\ N\text{———}O \end{matrix} + C_2H_5\cdot OH.$$

Phenylisoxazolon.

The formation of this compound is readily understood, if we suppose that dibenzoylacetic acid in alkaline solution is decomposed into benzoylacetic acid and benzoic acid. The former then reacts with hydroxylamine, forming phenylisoxazolon.

Experiments were then instituted on the action of phenylhydrazine on ethyl dibenzoylacetate. 2 grams of the pure substance was mixed with 2 grams of phenylhydrazine, and the mixture heated at 180° in a test-tube until all action had ceased. The product, which on cooling solidified, was powdered, washed with ether till free from oily impurity, dried on a porous plate, and recrystallised several times from benzene. The beautiful, white, silky substance thus obtained melted at 165—168°, and was found to consist of benzoylphenylhydrazine, $C_6H_5\cdot CO\cdot NH\cdot NH\cdot C_6H_5$. Analysis:—

0·2116 gram substance gave 25·6 c.c. N; $t = 22°$; bar. = 740 mm.

	Theory. $C_{13}H_{12}N_2O$.	Found.
N.....	13·21 per cent.	13·33 per cent.

In the formation of this substance, the ethyl dibenzoylacetate is evidently first hydrolysed with formation of benzoic and acetic acids, and the former then combines with the phenylhydrazine.

It is probable that, under other conditions, the direct product of the action of phenylhydrazine on ethyl dibenzoylacetate might be obtained, and further experiments on this subject are in progress.

Ethyl Dibenzoylmethylacetate, $(C_6H_5\cdot CO)_2C(CH_3)\cdot COOC_2H_5$.

This interesting substance was obtained in the following way:—1·6 grams of sodium wire was suspended in pure dry ether, 15 grams of ethyl methylbenzoylacetate, $C_6H_5\cdot CO\cdot CH(CH_3)\cdot COOC_2H_5$, added, the mixture allowed to stand until the sodium had entirely dissolved, and 12 grams of freshly distilled benzoyl chloride gradually added. After standing for two hours, water was added, the ethereal solution sepa-

rated, washed repeatedly with dilute sodium carbonate solution to remove any excess of benzoyl chloride, dried over calcium chloride, evaporated, and the residual oil, after standing over sulphuric acid under diminished pressure, analysed with the following result:—

0·2102 gram substance gave 0·1134 gram H_2O and 0·5618 gram CO_2.

	Theory. $C_{19}H_{18}O_4$.	Found.
C	73·55 per cent.	72·89 per cent.
H	5·81 ,,	5·99 ,,
O	20·64 ,,	21·12 ,,

Ethyl dibenzoylmethylacetate is a thick, yellowish oil, which, even on long standing, does not solidify; it is readily hydrolysed by boiling with alcoholic potash, with formation of benzoic acid and a neutral substance which is probably phenyl ethyl ketone, $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CH_3$, and all attempts to obtain the corresponding dibenzoylmethylacetic acid were fruitless. When ethyl dibenzoylmethylacetate is heated in a test-tube with phenylhydrazine at 180°, benzoylphenylhydrazine is produced. This substance, after repeated recrystallisation, melted at 165°, and gave the following results on analysis:—

0·2296 gram substance gave 2·64 c.c. N; $t = 15°$; bar. = 744 mm.
0·1630 ,, ,, 0·0836 gram H_2O and 0·4400 gram CO_2.

	Theory. $C_6H_5{\cdot}CO{\cdot}NH{\cdot}NH{\cdot}C_6H_5$.	Found.
C.....	73·58 per cent.	73·62 per cent.
H.....	5·66 ,,	5·70 ,,
N.....	13·20 ,,	13·18 ,,

Ethyl Benzylbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}CH(C_7H_7){\cdot}COOC_2H_5$.

This ethereal salt is readily prepared by treating the sodium compound of ethyl benzoylacetate with benzyl chloride in alcoholic solution, thus:—

$$C_6H_5{\cdot}CO{\cdot}CHNa{\cdot}COOC_2H_5 + C_7H_7Cl = C_6H_5{\cdot}CO{\cdot}CH(C_7H_7){\cdot}COOC_2H_5 + NaCl.$$

40 grams of ethyl benzoylacetate was dissolved in a solution of 5 grams of sodium in 50 grams of absolute alcohol, 27 grams of freshly-distilled benzyl chloride added, and the mixture heated in a reflux apparatus on a water-bath for two hours. The alcohol was then distilled off, water added, the product extracted three times with ether, the ethereal solution washed with water, dried over calcium chloride, evaporated, and the residual, yellowish oil purified by fractionation

under diminished pressure (80 mm.). After a considerable quantity of an oil of low boiling point had passed over, smelling strongly of benzyl ethyl ether, $C_6H_5 \cdot CH_2 \cdot OC_2H_5$, the thermometer rose rapidly to 265°, between which temperature and 270° a considerable quantity distilled.

The almost colourless oil thus obtained gave on analysis the following numbers :—

0·1617 gram substance gave 0·1075 gram H_2O and 0·4544 gram CO_2.

	Theory. $C_{18}H_{18}O_3$.	Found.
C	76·60 per cent.	76·64 per cent.
H	6·39 „	6·79 „
O	17·02 „	16·57 „

Ethyl benzylbenzoylacetate is a thick, slightly-yellowish oil, which does not solidify even on long standing; it resembles closely the corresponding methyl salt, prepared by Perkin and Colman (Trans., 1886, **49**, 155) from methyl benzoylacetate by treatment with sodium ethylate and benzyl chloride.

Hydrolysis of Ethyl Benzylbenzoylacetate. Formation of Benzylacetophenone, $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot C_6H_5$.

In order to examine the behaviour of ethyl benzylbenzoylacetate on hydrolysis, a quantity of this ethereal salt was dissolved in absolute alcohol, heated to boiling on a water-bath in a reflux apparatus, and then a dilute solution of potassium hydrate (3 mols.) added, drop by drop, from a dropping funnel; after digesting for one hour, the solution was allowed to cool; on standing for 24 hours, a crystalline substance separated, which was collected, washed with a little alcohol, recrystallised from this solvent, and the beautifully glistening, colourless plates thus obtained dried over sulphuric acid under reduced pressure, and analysed with the following result :—

0·1239 gram substance gave 0·0765 gram H_2O and 0·3882 gram CO_2.

	Theory. $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot C_6H_5$.	Found.
C	85·71 per cent.	85·53 per cent.
H.....	6·66 „	6·86 „
O.....	7·62 „	7·61 „

Benzylacetophenone melts at 70°. It is readily soluble in hot alcohol, benzene, and light petroleum; it crystallises from its hot solution in methyl alcohol or light petroleum in beautiful, glistening needles.

The alkaline filtrate from the crystals of benzylacetophenone was boiled till free from alcohol, filtered, acidified with hydrochloric acid, and extracted with ether. In this way a small quantity of an acid was extracted, which, on evaporating and subsequent recrystallisation of the residue from water, was obtained in colourless needles melting at 120°, and possessing the properties of benzoic acid, and the aqueous mother liquors from the benzoic acid, contained small quantities of a second acid, presumably phenylpropionic acid. The yield of ketone obtained by the above method is very good, approximately 80 per cent. of the theory; the formation of this ketone by the hydrolysis of ethyl benzylbenzoylacetate may be represented thus:—

$$C_6H_5\cdot CO\cdot CH(C_7H_7)\cdot COOC_2H_5 + 2KOH = C_6H_5\cdot CO\cdot CH_2\cdot CH_2\cdot C_6H_5 + K_2CO_3 + C_2H_5\cdot OH.$$

Oxime of Benzylacetophenone, $C_6H_5\cdot C(NOH)\cdot CH_2\cdot CH_2\cdot C_6H_5$.

This oxime was prepared by dissolving the pure ketone (2 grams) in methyl alcohol, adding an aqueous solution of 1·5 grams of hydroxylamine hydrochloride and an alcoholic solution of 3 grams of potassium hydrate, and allowing the mixture to stand for 24 hours. In order to isolate the product, the alcohol was removed by gentle evaporation, the oily oxime, which, however, rapidly solidifies, collected, washed with water, dried on a porous plate, and purified by recrystallisation from dilute alcohol.

The analysis gave the following numbers:—

0·2110 gram substance gave 11·4 c.c. N; $t = 11°$; bar. = 760 mm.

	Theory. $C_{15}H_{15}NO$.	Found.
N.....	6·22 per cent.	6·43 per cent.

Benzylacetophenoneoxime crystallises from dilute alcohol or light petroleum in colourless needles which melt at 82°. It is readily soluble in alcohol, benzene, chloroform, and hot light petroleum, sparingly in water and cold light petroleum; it is also insoluble in alkalis and dilute acids.

Reduction of Benzylacetophenone: Diphenyl Propyl Alcohol, $C_6H_5\cdot CH(OH)\cdot CH_2\cdot CH_2\cdot C_6H_5$.

This reduction was carried out by dissolving the pure ketone in ether, floating the solution on water, and cautiously adding about twice the calculated quantity of sodium in small quantities at a time. The ethereal solution was separated, washed with water, dried over calcium chloride, evaporated, and the residual thick oil purified by

fractionation under diminished pressure (70 mm.). In this way a fair quantity of a thick, colourless oil was obtained, boiling at about 240° (70 mm.); but there was a considerable residue left in the retort, which probably consists of the corresponding pinacone.

The analysis of diphenyl propyl alcohol gave the following numbers:—

0·1576 gram substance gave 0·1128 gram H_2O and 0·4886 gram CO_2.

	Theory. $C_{15}H_{16}O$.	Found.
C	84·90 per cent.	84·53 per cent.
H	7·55 „	7·90 „
O	7·55 „	7·57 „

Diphenyl propyl alcohol is a thick, colourless oil, which, even on long standing, showed no signs of crystallising.

α-Ethyl-β-phenylhydroxypropionic Acid,
$C_6H_5{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH$.

This acid may be readily prepared from ethyl ethylbenzoylacetate by reduction with sodium amalgam, thus:—

$$C_6H_5{\cdot}CO{\cdot}CH(C_2H_5){\cdot}COOC_2H_5 + H_2 + H_2O = C_6H_5{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH + C_2H_5{\cdot}OH.$$

The pure ethereal salt was dissolved in dilute alcohol, and the solution treated in a flat dish with a considerable excess of $2\frac{1}{2}$ per cent. sodium amalgam, in small quantities at a time. The product was separated from the mercury, heated on a water-bath till free from alcohol, acidified with dilute hydrochloric acid, and extracted six times with ether. The ethereal solution, after drying over calcium chloride and evaporating, deposited a thick, almost colourless oil, which, even on long standing, showed no signs of crystallising.

In order to purify this crude product, it was dissolved in an excess of barium hydrate solution, the excess of baryta removed by passing a rapid current of carbon dioxide through the boiling solution, and the filtrate acidified with hydrochloric acid, and extracted six times with ether. The ethereal solution, after being dried over calcium chloride, was evaporated, and the residual colourless oil allowed to stand for some days over sulphuric acid under reduced pressure. The crystalline cake which gradually formed was roughly purified by spreading it on a porous plate, and subsequently recrystallising it from carbon bisulphide.

The analysis gave the following results:—

0·1230 gram substance gave 0·0825 gram H_2O and 0·3074 gram CO_2.

	Theory. $C_6H_5{\cdot}CH(OH){\cdot}CH(C_2H_5){\cdot}COOH$.	Found.
C	68·04 per cent.	68·15 per cent.
H	7·22 ,,	7·45 ,,
O	24·74 ,,	24·40 ,,

α-Ethyl-β-phenylhydroxypropionic acid melts at 110—112°. It is readily soluble in benzene, alcohol, and boiling water, but only sparingly in light petroleum.

The *silver salt* was prepared by adding silver nitrate to a moderately concentrated neutral solution of the ammonium salt; it is a white, amorphous precipitate sparingly soluble in water. Analysis:—

0·2619 gram substance left on ignition 0·0934 gram Ag.

	Theory. $C_{11}H_{13}AgO_3$.	Found.
Ag.....	35·80 per cent.	35·66 per cent.

Action of Heat on α-Methyl-β-phenylhydroxypropionic Acid: Formation of Allylbenzene, $C_6H_5{\cdot}CH{:}CH{\cdot}CH_3$.

When heated at a high temperature, α-methyl-β-phenylhydroxypropionic acid is decomposed with formation of water, carbonic anhydride, and allylbenzene, thus:—

$$C_6H_5{\cdot}CH(OH){\cdot}CH(CH_3){\cdot}COOH = C_6H_5{\cdot}CH{:}CH{\cdot}CH_3 + CO_2 + H_2O.$$

In studying this decomposition, the pure acid* was heated in a small Würtz flask at 280° until the evolution of carbonic anhydride had entirely ceased, the residue rapidly distilled, the colourless distillate dried over potassium carbonate, and submitted to very careful fractional distillation. A considerable quantity of a colourless oil was thus obtained, boiling constantly at 174—175°, but which gave no satisfactory result on analysis.

The whole was therefore redistilled over sodium, the operation being rapidly conducted, in order, as far as possible, to prevent polymerisation, the distillate refractioned, and the oil boiling at 174—175° analysed with the following result:—

0·1238 gram substance gave 0·0947 gram H_2O and 0·4130 gram CO_2.

	Theory. $C_6H_5{\cdot}CH{:}CH{\cdot}CH_3$.	Found.
C.....	91·52 per cent.	90·98 per cent.
H.....	8·47 ,,	8·49 ,,

* This acid melts at 95°, and not at 124—125°, as previously stated (Trans., 1886, **49**, 160).

Allylbenzene has been obtained by several methods (Beilstein, *Handbuch*, 1888, ii, 126), but the boiling point is variously given as 164·5° and 174—175°. In order, therefore, to be certain of the identity of the substance we had obtained, it was converted into the dibromide by adding to the solution in chloroform the calculated quantity of bromine. On allowing it to evaporate at ordinary temperatures, colourless needles separated, which were dried on a porous plate and analysed with the following result :—

0·2388 gram substance gave 0·3023 gram AgBr.

	Theory. $C_6H_5{\cdot}CHBr{\cdot}CHBr{\cdot}CH_3$.	Found.
Br.....	53·95 per cent.	53·86 per cent.

This dibromide melts at 66·5°, and agrees in its properties with $\alpha\beta$-dibromopropylbenzene (Beilstein, *Handbuch*, 1888, ii, 50).

Condensation of Ethyl Benzoylacetate with Furfuraldehyde. Ethyl Furfuralbenzoylacetate, $C_6H_5{\cdot}CO{\cdot}C(:CH{\cdot}C_4H_3O){\cdot}COOC_2H_5$ (?).

This condensation takes place readily when a mixture of ethyl benzoylacetate (10 grams) and furfuraldehyde (5 grams) is heated with excess of acetic anhydride for three hours in a sealed tube at 150°. The resulting brownish-coloured product was freed from acetic anhydride and acetic acid by fractionation, and the residual crude condensation product distilled from a small retort under diminished pressure. The thick, dark-coloured, oily distillate, on standing, gradually solidified to a mass of brownish crystals; these were first roughly purified by contact with a piece of porous plate, and then recrystallised twice from methyl alcohol.

The beautiful, glistening, tabular crystals thus obtained gave on analysis the following numbers :—

0·1598 gram substance gave 0·0760 gram H_2O and 0·4112 gram CO_2.

	Theory. $C_{16}H_{14}O_4$.	Found.
C	71·11 per cent.	71·06 per cent.
H	5·18 „	5·34 „
O	23·71 „	23·60 „

Ethyl furfuralbenzoylacetate melts at 68°. It is readily soluble in alcohol and benzene, but only sparingly in light petroleum.

It crystallises from methyl alcohol in remarkably lustrous, four-sided, tabular prisms, which in appearance closely resemble the corresponding benzal compound (Trans., 1885, **47**, 260).

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, October*, 1890. Vol. LVII.]

DIPHENYLFURFURAN.

By W. H. Perkin, Jun., Ph.D., F.R.S., and Aug. Schloesser, Ph.D., M.Sc.

The constitution of carbuvic acid (carbopyrotritartaric acid) and uvic acid (pyrotritartaric acid) has, since the discovery of these acids by Harrow (Trans., 1878, 425), been the subject of most careful investigation.

Harrow first obtained these acids by boiling ethyl diacetylsuccinate, $\begin{matrix}CH_3\cdot CO\cdot CH\cdot COOEt\\ CH_3\cdot CO\cdot CH\cdot COOEt\end{matrix}$, with dilute sulphuric acid:—

$$C_{12}H_{18}O_6 + H_2O = \underset{\text{Carbuvic acid.}}{C_8H_8O_5} + 2C_2H_5\cdot OH.$$

$$C_8H_8O_5 = \underset{\text{Uvic acid.}}{C_7H_8O_3} + CO_2.$$

Knorr (*Ber.*, **17**, 2866) subsequently obtained the ethereal salt of carbuvic acid directly from ethyl diacetylsuccinate by the action of concentrated sulphuric acid:—

$$\begin{matrix}CH_3\cdot CO\cdot CH\cdot COOEt\\ CH_3\cdot CO\cdot CH\cdot COOEt\end{matrix} = C_8H_6O_5Et_2 + H_2O.$$

Paal (*Ber.*, **17**, 2765) showed that ethyl acetonylacetoacetate, when warmed with concentrated hydrochloric acid, yielded ethyl uvate, thus:—

$$\begin{matrix}CH_3\cdot CO\cdot CH\cdot COOEt\\ CH_3\cdot CO\cdot CH_2\end{matrix} = C_7H_7O_3Et + H_2O.$$

Arguing from these and other facts, Knorr and Paal concluded that carbuvic and uvic acids are furfuran-derivatives, the former being the di-, the latter the mono-carboxylic acid of dimethylfurfuran.

The formation of ethyl uvate, for example, from ethyl acetonyl-acetoacetate would be represented by the equation

$$\begin{array}{l}CH_3\cdot CO\cdot CH\cdot COOEt\\ \quad\quad\quad|\\ CH_3\cdot CO\cdot CH_2\end{array} = \begin{array}{l}CH_3\cdot C(OH):C\cdot COOEt\\ \quad\quad\quad\quad\quad|\\ CH_3\cdot C(OH):CH\end{array}$$

(Stable form). (Labile form).

$$\begin{array}{l}HC\text{—}C\cdot COOEt\\ \quad\|\quad\quad\|\\ CH_3\cdot C\quad C\cdot CH_3\\ \quad\quad\diagdown\quad\diagup\\ \quad\quad\quad O\end{array} + H_2O.$$

Ethyl uvate (dimethylfurfurancarboxylate).

Uvic acid was subsequently obtained by Fittig (*Ber.*, **18**, 3410, **21**, 2134), from methronic acid, by the elimination of carbon dioxide. Methronic acid is formed by the condensation of ethyl acetoacetate with sodium succinate in the presence of acetic anhydride.

Fittig (*Annalen*, **250**, 71) is of the opinion that in this reaction a sodium salt, $\begin{array}{l}CH_3\cdot C\text{—}CH\cdot COONa\\ \quad\|\quad\quad|\\ COOEt\cdot CH\quad CH_2\cdot COOH\end{array}$, is first formed, and this then loses 1 mol. H_2O, forming the sodium ethyl salt of methronic acid. Methronic and uvic acids would therefore have the following formulæ:—

$$\begin{array}{l}CH_3\cdot C\text{——}CH\cdot COOH\\ \quad\|\quad\quad|\\ COOH\cdot C\cdot CO\cdot CH_2\end{array} \quad , \quad \begin{array}{l}CH_3\cdot C\text{——}CH\cdot COOH\\ \quad\|\quad\quad|\\ HC\cdot CO\cdot CH_2\end{array}$$

Methronic acid. Uvic acid.

It will be seen at a glance that Fittig's formula for uvic acid differs very materially from that proposed by Paal and Knorr; the former supposes this acid to be a derivative of a closed carbon chain, $\begin{array}{l}CH_3\cdot C\text{——}CH_2\\ \quad\|\quad\quad|\\ \quad CH\cdot CO\cdot CH_2\end{array}$, whereas according to the latter, this acid is a derivative of dimethylfurfuran, $\begin{array}{l}HC\text{—}CH\\ \|\quad\|\\ CH_3\cdot C\quad C\cdot CH_3\\ \quad\diagdown\quad\diagup\\ \quad\quad O\end{array}$.

Fittig explains Knorr's synthesis of ethyl carbuvate from ethyl diacetylsuccinate and Paal's synthesis of ethyl uvate from ethyl acetonylacetoacetate on the assumption that in both cases a simple mesityl oxide condensation takes place, thus:—

$$\begin{array}{l}CH_3\cdot CO\cdot CH\cdot COOEt\\ \quad\quad\quad|\\ CH_3\cdot CO\cdot CH_2\end{array} = \begin{array}{l}CH_3\cdot C\text{——}CH\cdot COOEt\\ \quad\|\quad\quad|\\ \quad HC\cdot CO\cdot CH_2\end{array} + H_2O.$$

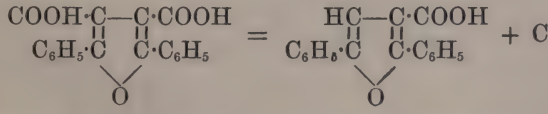
Ethyl acetonylacetoacetate. Ethyl uvate.

The general behaviour of these substances towards reagents, and particularly the fact that they do not combine with phenylhydrazine or hydroxylamine, favours very strongly the view that they are furfuran-derivatives; but, on the other hand, it is difficult, as Fittig points out, to explain the formation of dimethylfurfuran-derivatives by the condensation of succinic acid with ethyl acetoacetate.

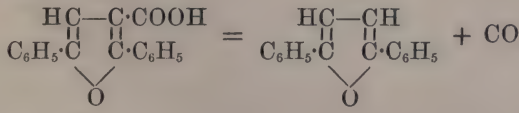
In a paper published some time since (Trans., 1885, **47**, 271; compare also Trans., 1886, **49**, 166—171), it was shown, by one of us, that ethyl dibenzoylsuccinate, $\begin{matrix} C_6H_5\cdot CO\cdot CH\cdot COOEt \\ C_6H_5\cdot CO\cdot CH\cdot COOEt \end{matrix}$, when dissolved in concentrated sulphuric acid, underwent condensation, giving rise to an ethereal salt, $C_{22}H_{20}O_5$, which in its reactions showed great similarity to ethyl carbuvate. On hydrolysis, it was converted into a bibasic acid (diphenylfurfurandicarboxylic acid),* $C_{18}H_{12}O_5$, which corresponded to carbuvic acid; from which, however, it appeared to differ in that when heated it yielded an anhydride, whereas carbuvic acid, under similar treatment, is decomposed into uvic acid and carbonic anhydride.

At that time, owing to the difficulty in obtaining material, these experiments were left unfinished; in view, however, of the importance of assigning the correct formulæ to these derivatives, we have again taken up the subject and now beg to lay the results of our experiments before the Society.

The action of heat on diphenylfurfurandicarboxylic acid has now been carefully investigated, and our experiments have shown that this acid when rapidly and strongly heated is readily decomposed with evolution of carbon dioxide and formation of diphenylfurfuran-monocarboxylic acid—



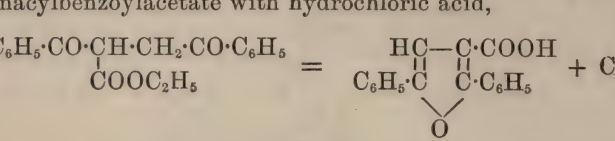
This acid is again readily decomposed into carbon dioxide and diphenylfurfuran, thus:—



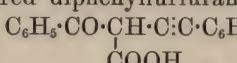
Diphenylfurfuranmonocarboxylic acid has already been prepared by

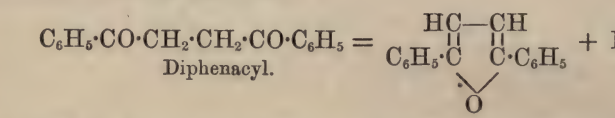
* In this paper, these acids are considered as furfuran-derivatives for the sake of simplicity.

Kapf and Paal (*Ber.*, **21**, 1489 and 3054) by acting on ethyl phenacylbenzoylacetate with hydrochloric acid,



and possesses the same melting point (217°) and the same properties as the acid obtained from diphenylfurfurandicarboxylic acid.*

Paal also prepared diphenylfurfuran by heating phenylacetylenebenzoylacetic acid,  , or diphenacyl, with fuming hydrochloric acid at 130—150°,

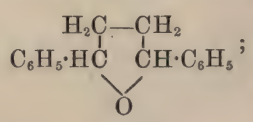


this substance being also identical with the diphenylfurfuran obtained by us.*

If diphenylfurfuran is submitted to the vapour of bromine, it is converted into a beautifully crystalline compound, $C_{16}H_{10}Br_4O$, which melts at 191°,

$$C_{16}H_{12}O + 3Br_2 = C_{16}H_{10}Br_4O + 2HBr,$$

and when treated with sodium and alcohol, diphenylfurfuran is readily reduced with formation of a variety of products depending on the amount of sodium employed. In studying this reaction, Paal (*Ber.*, **21**, 3057) obtained diphenyltetrahydrofurfuran,



but we found, on repeating this experiment, that if a large excess of sodium is employed, diphenylfurfuran takes up as many as eight atoms of hydrogen, forming octohydrodiphenylfuran, $C_{16}H_{20}O$, the two phenyl-groups being apparently partially reduced.

In preparing considerable quantities of diphenylfurfuran, a small quantity of a secondary product was obtained, which crystallised in yellow needles and on analysis gave numbers agreeing with the formula $C_{34}H_{20}O_4$. This substance is obviously formed by the con-

* Through the kindness of Dr. Paal, I have been enabled to institute a direct comparison of his and my derivatives, and have found them to be identical in every respect.

densation of two molecules of diphenylfurfuranmonocarboxylic acid, the reaction being similar to the formation of anthraquinone from benzoic acid,

$$2\,O<\begin{matrix}C(C_6H_5):CH\\ C(C_6H_5):C\cdot COOH\end{matrix} =$$

$$O<\begin{matrix}C(C_6H_5):C\cdot CO\cdot C:C(C_6H_5)\\ C(C_6H_5):C\cdot CO\cdot C:C(C_6H_5)\end{matrix}>O + 2H_2O.$$

Carbuvic acid.

In studying the action of heat on carbuvic acid, Paal (*Ber.*, **20**, 1086) isolated a substance, tetramethyluvinone,* which corresponds in every respect with the condensation-product just described; to this he gave the formula

$$O<\begin{matrix}C(CH_3):C\cdot CO\cdot C:C(CH_3)\\ C(CH_3):C\cdot CO\cdot C\ C(CH_3)\end{matrix}>O.$$

We propose to name our product tetraphenyluvinone.

In studying these results, it is obvious that whatever the constitution of carbuvic acid may be, the substances described above can only be furfuran-derivatives, because in the formation of these substances from ethylic dibenzoylsuccinate, owing to the absence of methyl-groups no mesityl oxide condensation, such as that suggested by Fittig, can take place.

As, however, the internal condensation of ethyl diacetylsuccinate runs so exactly parallel with that of ethyl dibenzoylsuccinate, and as in both cases products so exactly similar in properties are produced, it is extremely probable that carbuvic acid and diphenylfurfurandicarboxylic acid are similarly constituted.

Supposing methronic acid to be a furfuran-derivative, its formation from ethyl acetoacetate and succinic acid by Fittig's synthesis might be explained thus:—

I. In the first place, condensation takes place between the methylene-group of the ethyl acetoacetate and one carboxyl-group of the succinic acid, thus:—

$$CH_3\cdot CO\cdot CH_2\cdot COOC_2H_5 + COOH\cdot CH_2\cdot CH_2\cdot COOH =$$
$$\begin{matrix}CH_3\cdot CO\cdot CH\cdot COOC_2H_5\\ COOH\cdot CH_2\cdot CH_2\cdot CO\end{matrix} + H_2O.$$

* This substance was originally termed uvinone by Dr. Paal, but I have recently received a communication from him in which he agrees with me that the term uvinone is best applied to the parent-substance $O<\begin{matrix}CH:C\cdot CO\cdot C:CH\\ CH:C\cdot CO\cdot C:CH\end{matrix}>O$ and that consequently his compound should be termed tetramethyluvinone.

II. This intermediate product, under the influence of the dehydrating agents employed, loses 1 mol. H_2O, thus:—

$$\begin{matrix} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ COOH\cdot CH_2\cdot CH_2\cdot CO \end{matrix} = \begin{matrix} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ COOH\cdot CH_2\cdot C\vdots C \end{matrix} + H_2O.$$

III. A substance of this constitution is, as Paal has repeatedly shown, readily converted into a furfuran-derivative, thus:—

$$\begin{matrix} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ COOH\cdot CH_2\cdot C\vdots C \end{matrix} + H_2O = \begin{matrix} CH_3\cdot CO\cdot CH\cdot COOC_2H_5 \\ COOH\cdot CH_2\cdot CO\cdot CH_2 \end{matrix}$$

$$= \begin{matrix} HC{-}C\cdot COOC_2H_5 \\ COOH\cdot CH_2\cdot C \quad C\cdot CH_3 \\ \qquO \end{matrix}.$$

According to this explanation, methronic acid would be represented by the formula

$$\begin{matrix} COOH\cdot C{-}CH \\ CH_3\cdot C \quad C\cdot CH_2\cdot COOH \\ \qquO \end{matrix}.$$

This formula fully explains the isomerism of methronic and carbuvic acids, and also the fact that the former acid, on heating, is converted into uvic acid and carbon dioxide. Should the above prove to be the correct explanation of the formation of methronic acid and other acids obtained by similar reactions by Fittig, this will be an interesting example of the transference of an oxygen-atom from one carbon-atom to the neighbouring carbon-atom, thus:—

$$\begin{matrix} \cdot CH_2\cdot CO\cdot \\ \text{or} \\ \cdot CH\vdots C(OH)\cdot \end{matrix} = \cdot C\vdots C\cdot + H_2O = \begin{matrix} \cdot CO\cdot CH_2\cdot \\ \text{or} \\ \cdot C(OH)\vdots CH\cdot \end{matrix}.$$

This simultaneous splitting off and reverse addition of the elements of water was first suggested by Baeyer (*Ber.*, **3**, 70).

Ethyl Dibenzoylsuccinate, $\begin{matrix} C_6H_5\cdot CO\cdot CH\cdot COOC_2H_5 \\ C_6H_5\cdot CO\cdot CH\cdot COOC_2H_5 \end{matrix}$.

This ethereal salt was first prepared by the action of iodine on the dry sodium compound of ethyl benzoylacetate suspended in ether (Trans., 1885, **47**, 263).

As it was necessary in this research to prepare considerable quantities of this substance, numerous experiments were first made

with the view of finding the conditions which gave the best yield. As the result of these the following method was ultimately adopted.

2·5 grams of sodium, in the form of very fine wire, was placed in a flask containing 500 c.c. of absolute ether, and 20 grams of ethyl benzoylacetate was then added in small portions at a time, the contents of the flask being carefully cooled during the operation by a stream of cold water. The sodium compound of ethyl benzoylacetate soon separated out, and the mass ultimately became quite thick. The action is allowed to go on for about three hours, the contents of the flask being violently agitated from time to time, in order to prevent the particles of sodium from being covered with the white sodium compound and thus rendered inactive. 14 grams of iodine, dissolved in absolute ether, was now allowed to run in slowly from a dropping funnel, the flask being well agitated during the operation. The resulting slightly brownish solution was mixed with water, the slight excess of iodine removed by the addition of a few drops of sulphurous acid, the ethereal layer separated, washed once with water, dried over calcium chloride, and the ether distilled off. The slightly yellowish oily residue, on standing, almost completely solidified to a mass of crystals of crude ethyl dibenzoylsuccinate. This crude product is best purified by trituration in a mortar with cold methylated spirit, in which the crystals are very sparingly soluble, separation of the dark-coloured mother liquor by filtration, and recrystallisation of the almost colourless residue from boiling purified methylated spirit.

100 grams of ethyl benzoylacetate by this process yielded from 65 to 70 grams of pure ethyl dibenzoylsuccinate.

Diphenylfurfurandicarboxylic Acid, $\begin{matrix} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ \| \qquad\quad \| \\ COOH\cdot C-C\cdot COOH. \end{matrix}$

Solution in sulphuric acid converts ethyl dibenzoylsuccinate quantitatively into ethyl furfurandicarboxylate, thus :—

$$\begin{matrix} C_6H_5\cdot CO\cdot CH\cdot COOC_2H_5 \\ | \\ C_6H_5\cdot CO\cdot CH\cdot COOC_2H_5 \end{matrix} - H_2O = \begin{matrix} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ \| \qquad\quad \| \\ COOC_2H_5\cdot C-C\cdot COOC_2H_5 \end{matrix}.$$

The details of this operation have already been given (Trans., 1886, **49**, 166). In a number of cases it was noticed that the solution of ethyl dibenzoylsuccinate in concentrated sulphuric acid acquired in the first place a deep brownish colour, which on standing for 12 hours gradually became green, and, lastly, of an intense indigo-blue.

The pure ethereal salt was hydrolysed by boiling on a water-bath, for about 15 minutes, with twice the calculated quantity of alcoholic potash. On mixing the ethereal salt with alcoholic potash, the

very sparingly soluble potassium salt of the bibasic acid separates out almost immediately (compare carbopyrotritartaric acid), in glittering needles. These are brought into solution by the addition of water, the excess of alcohol removed by evaporation, and the bibasic acid precipitated by the addition of an acid. The precipitate is collected, washed with water, and purified by recrystallisation from methylated spirit.

Diphenylfurfurandicarboxylic acid melts at 238°, and when strongly heated splits up into diphenylfurfuranmonocarboxylic acid and carbon dioxide, thus :—

$$\begin{array}{l} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ COOH\cdot C\!-\!C\cdot COOH \end{array} = \begin{array}{l} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ COOH\cdot C\!-\!CH \end{array} + CO_2.$$

The 1 : 2 position of the carboxyl-groups in diphenylfurfurandicarboxylic acid is clearly proved by the ease with which this acid is converted into its anhydride. This interesting compound has already been prepared in small quantities (Trans., 1885, **47**, 268); but in view of its importance in discussing the formula of diphenylfurfurandicarboxylic acid, we have again prepared and analysed this substance.

A beautiful specimen of the anhydride, twice recrystallised from acetic anhydride, gave the following results on analysis :—

0·1357 gram substance gave 0·3691 gram CO_2 and 0·0428 gram H_2O.

	Theory for $C_{18}H_{10}O_4$.	Found.
C	74·48 per cent.	74·17 per cent.
H	3·45 „	3·50 „
O	22·07 „	22·33 „

The properties of this anhydride have already been given (*loc. cit.*, p. 269).

Diphenylfurfuranmonocarboxylic Acid, $\begin{array}{l} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ CH\cdot C\cdot COOH \end{array}$.

In preparing this acid, pure diphenylfurfurandicarboxylic acid is heated in a round-bottomed flask, by a bath of fusible metal, until it melts, and the temperature is then gradually raised until a rapid evolution of carbon dioxide takes place. After heating for about five minutes, the effervescence slackens considerably, when the mass is poured into hot dilute sodium hydrate solution, heated nearly to boiling, in order to prevent the sparingly soluble sodium salt of the monocarboxylic acid from separating, and filtered through a hot water funnel. A considerable quantity of a dark-brownish substance

remains on the filter paper; this consists of crude diphenylfurfuran, and will be referred to later on. On acidifying the dark-coloured solution of the sodium salt, a white, crystalline substance is precipitated, which consists for the most part of diphenylfurfuranmonocarboxylic acid, mixed with varying quantities of unchanged bibasic acid. This was collected, washed with water, dried on a porous plate in a water-oven, and repeatedly extracted with small quantities of boiling benzene, in which the bibasic acid is very sparingly soluble. The solution on standing deposited the new acid in slender, white needles, which, after repeated recrystallisation from benzene, were readily obtained pure. The analysis gave the following numbers:—

0·1727 gram substance gave 0·4901 gram CO_2 and 0·0736 gram H_2O.

	Theory. $C_{17}H_{12}O_3$.	Found.
C	77·27 per cent.	77·42 per cent.
H	4·54 „	4·73 „
O	18·18 „	18·85 „

Diphenylfurfuranmonocarboxylic acid melts at about 214—217°. It is almost insoluble in water and light petroleum, readily soluble in boiling alcohol, acetic acid, and benzene.

The basicity of this acid was determined by titration with a standard solution of potassium hydrate.

0·6470 gram of acid required for neutralisation 24·8 c.c. of potassium hydrate solution, 1 c.c. of which contained 0·002786 gram KOH.

The amount of KOH used was therefore 0·06909 gram, whereas theory requires for a monobasic acid $C_{17}H_{12}O_3$, 0·06861 gram. The *silver salt* was prepared by dissolving the acid in a slight excess of dilute ammonia, allowing the solution to stand over sulphuric acid till neutral, and then precipitating with silver nitrate. It is a white, insoluble powder, which is only very slowly affected by light. The analysis of the salt dried at 100° gave the following numbers:—

0·2042 gram substance gave 0·0602 gram Ag.

	Theory. $C_{17}H_{11}O_3Ag$.	Found.
Ag	29·11 per cent.	29·48 per cent.

Experiments were next instituted with the object of demonstrating the absence of a hydroxyl- or carbonyl-group in diphenylfurfurancarboxylic acid.

a. 2 grams of the pure acid was boiled for three to four hours with an excess of acetic anhydride on a reflux apparatus. The acid soon dissolved, but no other change was noticed. After distilling off the

greater bulk of the anhydride, water was added, and the whole allowed to stand. The white, crystalline precipitate melted at 215°, and was found to be unaltered diphenylfurfuranmonocarboxylic acid.

b. 0·5 gram of pure acid was dissolved in an excess of potassium hydrate solution, 0·2 gram of hydroxylamine hydrochloride, dissolved in a little water, added, and the product allowed to stand for 48 hours. The solution was then acidified with dilute hydrochloric acid, the precipitate collected, washed, and dried at 100°. Its melting point was found to be 215—217°, and it was therefore unchanged acid.

Diphenylfurfurancarboxylic acid, as described above, is identical with $\alpha\alpha'$-diphenylfurfuran-β-carboxylic acid obtained by Paal (*Ber.*, **21**, 1489) by boiling phenylacetylenebenzoylacetic acid with alcohol and fuming hydrochloric acid. In addition to the properties given above, Paal noticed that the acid on oxidation gives a quantitative yield of benzoic acid. An account of the salts of this acid, including the ethyl salt ($C_{19}H_{16}O_3$, m. p. 82°), is also given.

Action of Bromine on Diphenylfurfurancarboxylic Acid.

The finely divided acid was exposed under a bell-jar to the fumes of bromine. The acid first appeared to melt, but after some hours it again completely solidified. The residual darkly-coloured mass was placed over soda-lime to remove excess of bromine, and thus obtained as a pinkish, extremely insoluble powder, which could not be obtained in a crystalline condition. It was repeatedly extracted with small quantities of hot alcohol, and the resulting colourless powder analysed, with the following result:—

0·1536 gram substance gave 0·1993 gram AgBr.

	Theory. $C_{17}H_{12}O_3Br_4$.	Found.
Br	54·98 per cent.	55·34 per cent.

Judging from the results obtained in our experiments on the action of bromine on diphenylfurfuran, it is extremely probable that the brominated acid has the constitution—

$$\begin{array}{l} C_6H_5\cdot BrC\cdot O\cdot CBr\cdot C_6H_5 \\ \quad\quad | \quad\quad\quad | \\ \quad BrHC-CBr\cdot COOH \end{array}.$$

Diphenylfurfuran, $\begin{array}{l} C_6H_5\cdot C\cdot O\cdot C\cdot C_6H_5 \\ \quad\quad || \quad\quad || \\ \quad\quad CH\cdot CH \end{array}$.

This substance is formed, together with diphenylfurfuranmonocarboxylic acid, by the action of heat on diphenylfurfurandicarboxylic acid. On treating the product of the reaction with dilute sodium

hydrate (see above), diphenylfurfuran is left behind as a brownish, crystalline mass. This was washed well with water, dried on a porous plate in a desiccator, and repeatedly extracted with boiling light petroleum (b. p. 70—90). By this means diphenylfurfuran is dissolved, leaving a varying quantity of a very sparingly soluble yellow substance, which will be described below.

The dark-coloured solution is evaporated, the residue transferred to a small retort, and very rapidly distilled under reduced pressure (50 mm.). The yellowish distillate is dissolved in a little boiling light petroleum, from which solvent, on cooling, pure diphenylfurfuran separates in colourless, glittering, fern-like crystals.

The analysis gave the following results:—

0·1592 gram substance gave 0·5086 gram CO_2 and 0·0787 gram H_2O.

	Theory. $C_{16}H_{12}O$.	Found.
C	87·27 per cent.	87·13 per cent.
H	5·46 „	5·49 „
O	7·27 „	7·38 „

Diphenylfurfuran melts at 88—89°, and has all the properties ascribed to this substance by Paal, who, however, gives the melting point as 91°.

Tetrabromodiphenylfurfuran, $C_{16}H_{10}Br_4O$.

In order to study the action of bromine on diphenylfurfuran, the finely divided substance was spread out on a sheet of glass, and exposed under a bell-jar to the vapours of bromine for 24 hours. On opening the bell-jar, it was noticed that considerable quantities of hydrogen bromide had been produced. The dark-coloured residue was placed over soda-lime till free from excess of bromine, and then once or twice recrystallised from benzene.

In this way beautiful, thin, colourless, satiny needles were obtained, which on analysis gave the following numbers:—

I. 0·1948 gram substance gave 0·0326 gram H_2O and 0·2580 gram CO_2.

II. 0·1834 gram substance gave 0·0302 gram H_2O and 0·2380 gram CO_2.

III. 0·2078 gram substance gave 0·2922 gram AgBr.

IV. 0·2190 gram „ 0·3061 gram AgBr.

	Theory. $C_{16}H_{10}Br_4O$.	Found. I.	II.	III.	IV.	
C.....	35·69 p. c.	36·12	35·39	—	—	p. c.
H.....	1·85 „	1·86	1·82	—	—	„
Br	59·48 „	—	—	59·81	59·47	„

Tetrabromodiphenylfurfuran melts at 190—191°. It is readily soluble in boiling benzene, carbon bisulphide, and acetic acid; sparingly soluble in hot alcohol and light petroleum. When quickly heated, in small quantities, it sublimes apparently unchanged. The substance is indeed characterised by its extreme stability; even boiling with zinc-dust and acetic acid seems to have little influence on it.

Reduction of Diphenylfurfuran.

In his experiments on diphenylfurfuran, Paal (*Ber.*, **21**, 3057) found that when this substance is reduced in alcoholic solution by sodium it is converted into tetrahydrodiphenylfurfuran, $C_{16}H_{16}O$ (a colourless oil boiling at 320—322°).

We have carried out a number of experiments on this same subject, and find that in this reaction a variety of products are formed, according to the amount of sodium used. Thus, if slightly more than the theoretical quantity for 4 atoms of hydrogen is employed, an oil is obtained which has properties very similar to those assigned by Paal to tetrahydrodiphenylfurfuran; this on analysis gives numbers agreeing fairly well with this formula:—

0·1530 gram substance gave 0·1061 gram H_2O and 4802 gram CO_2.

	Theory. $C_{16}H_{16}O$.	Found.
C	85·71 per cent.	85·53 per cent.
H.....	7·14 „	7·69 „

If, on the other hand, a large excess of sodium is employed, diphenylfurfuran takes up 8 atoms of hydrogen, and is converted into octohydrodiphenylfurfuran. The details of the preparation of this substance are the following.

Pure diphenylfurfuran (10 grams) is dissolved in boiling absolute alcohol (300 grams), and a large excess of sodium (25—30 grams) added as quickly as possible, a little more alcohol being added from time to time if necessary. The product is mixed with water, the alcohol boiled off, and the residue extracted two or three times with ether. The ethereal solution is washed with water, dried over calcium chloride, the ether distilled off, and the residual, almost colourless oil purified by repeated fractionation under diminished pressure.

Two preparations were made and analysed.

I. The oil boiled at 210—220°, under a pressure of 40 mm.
0·1570 gram substance gave 0·1236 gram H_2O and 0·4842 gram CO_2.

II. The oil boiled at 245—250°, under a pressure of 110 mm.
0·1596 gram substance gave 0·4940 gram CO_2 and 0·1276 gram H_2O.

	Theory. $C_{16}H_{20}O$.	Found. I.	Found. II.
C	84·21 per cent.	84·11	84·41 per cent.
H	8·77 „	8·75	8·84 „

Tetraphenyluvinone, $C_{34}H_{20}O_4$.

This substance is produced in small quantity in the preparation of diphenylfurfuran, and, being very insoluble, remains behind after extracting the crude product with light petroleum or benzene, as described above. The crude yellow residue is readily purified by recrystallisation from boiling xylene.

Analysis:—

0·1513 gram substance gave 0·0575 gram H_2O and 0·4590 gram CO_2.

	Theory. $C_{34}H_{20}O_4$.	Found.
C	82·93 per cent.	82·74 per cent.
H	4·07 „	4·22 „
O	13·00 „	13·04 „

Tetraphenyluvinone crystallises from xylene, in which it is only sparingly soluble, in thin, brilliant, yellow needles, which are often grouped together in tufts. It does not melt at 280°. It is very sparingly soluble in boiling alcohol, benzene, acetic acid, and most other organic solvents. On exposure to light, the crystals rapidly become of a deep orange colour.

Prolonged boiling with zinc-dust and acetic acid dissolves the substance, forming a reddish solution from which water precipitates a salmon-coloured, amorphous precipitate. Fusion with potash causes the substance to char.

The following property is highly characteristic of tetraphenyluvinone. If the smallest trace of the substance be added to concentrated sulphuric acid, a most intense dark-green solution is produced, which possesses a most magnificent dark, brick-red fluorescence. If the solution be strongly heated, the green colour gradually changes to a pure blue without influencing the fluorescence. A drop of nitric acid added to the sulphuric acid solution produces a red coloration

without fluorescence. The colour and fluorescence of the sulphuric acid solution instantly disappear on adding water.

Experiments on the absorption spectrum and general optical properties of the solution are in progress.

Heriot Watt College, Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

[*Reprinted from the Journal of the Chemical Society, June*, 1890. Vol. LVII.]

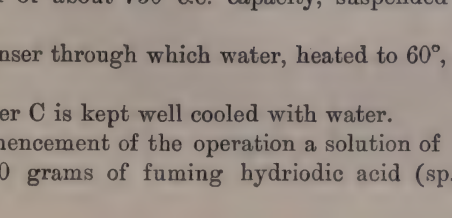
NOTE ON THE PREPARATION OF PYROCATECHOL.

By W. H. Perkin, Jun., Ph.D.

In the course of some experiments on derivatives of pyrocatechol, my attention was drawn to the high price of this substance (Kahlbaum's price is 4*s.* for 10 grams), and it appeared very desirable to endeavour to find some method by which this important product might be readily and cheaply prepared. Although this phenol is so expensive, its methyl ether guaiacol can be obtained for 20*s.* per kilo. and less; and experiments were therefore instituted with the object of ascertaining whether, under suitable conditions, a good yield of pyrocatechol might be obtained from guaiacol.

Baeyer (*Ber.*, **8**, 153) has shown that pyrocatechol may be obtained by saturating guaiacol, heated at 195—200°, with hydrogen iodide, and fractionating the product, but the yield obtained is small. By slightly modifying the conditions, that is, by using a solution of hydrogen iodide instead of the gas, I have found that an almost quantitative yield of pyrocatechol may be readily obtained.

The details of this method will be readily understood with the help of the following sketch of the apparatus employed, which was suggested by that of the one described by Zeisel for use in his experiments on the determination of methoxyl-groups (*Monats.*, **6**, 995).



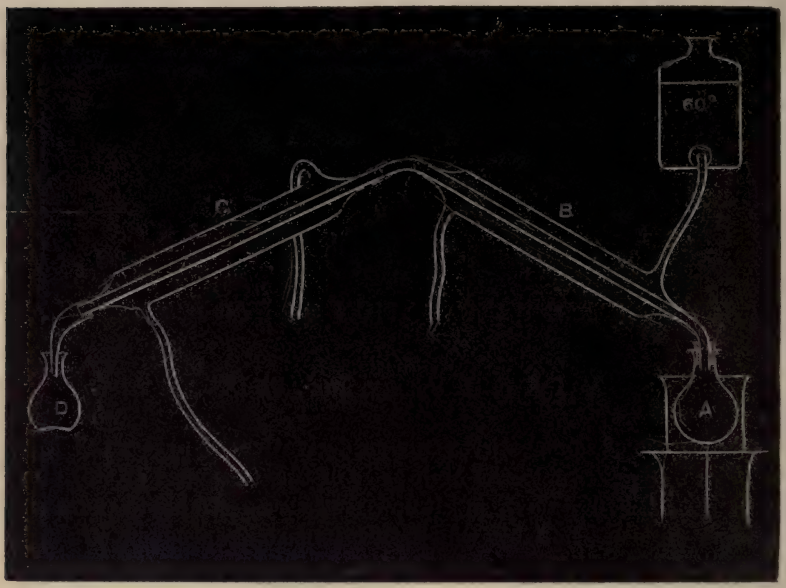
A is a flask of about 750 c.c. capacity, suspended in an oil- or glycerol-bath.

B is a condenser through which water, heated to 60°, is allowed to circulate.

The condenser C is kept well cooled with water.

At the commencement of the operation a solution of 100 grams of guaiacol in 150 grams of fuming hydriodic acid (sp. gr. 1·96) is

placed in the flask A, which is then fitted firmly to the condenser B, and very gradually heated to boiling. In a short time abundance of methyl iodide is given off, and this, after passing through B, condenses



in C, and collects in the flask D, which should contain a little water and be kept cold. The mixture is gently heated for one hour, allowed to cool slightly, mixed with more hydriodic acid (50—75 grams), and heated as before for one hour. It was found that 101 grams of slightly moist methyl iodide had distilled over, whereas theory requires 114 grams.

The product of the reaction was mixed with three times its volume of water, extracted six times with ether, the ethereal solution washed with a little water, decolorised with a little sulphurous acid, and dried over calcium chloride The ether was then distilled off, and the residual dark-coloured oil purified by rapid fractionation. As soon as the last traces of ether had passed over, the thermometer rose at once to 230°, between which temperature and 255° the whole distilled as a colourless oil which, on cooling, solidified to a hard cake of crystals of pyrocatechol. The yield obtained was 85 grams or 96 per cent. of the theoretical.

In order to further purify this product, it was melted, poured into 100 c.c. of boiling benzene, and the solution allowed to stand over night. The crystals were drained, washed with a little benzene,

dried on a porous plate over sulphuric acid, and analysed with the following result:—

0·1749 gram substance gave 0·0900 gram H_2O and 0·4211 gram CO_2.

	Theory. $C_6H_4(OH)_2$.	Found.
C	65·45	65·60
H	5·45	5·72
O	29·09	28·68

The substance melted at 104°, and possessed all the properties of pyrocatechol.

The crystals obtained weighed 63 grams, without taking into account what remained in the mother liquor.

While engaged on this subject, experiments were made on the action of hydrochloric acid on guaiacol. As, however, guaiacol is almost insoluble in hydrochloric acid, simple boiling did not appear to produce much effect on the oil; but decomposition readily sets in if the liquids are heated together under pressure. 30 grams of guaiacol and 50 c.c. of ordinary concentrated hydrochloric acid were heated in a sealed tube for four hours at 170—180°. The tube, after cooling, was wrapped in a cloth, inverted, the capillary inserted into a flask, and broken at the tip; in this way the whole contents were readily transferred to the flask; otherwise, owing to the pressure in the tube and the tendency of the liquid to froth, loss can scarcely be avoided.

The product was mixed with water, extracted with ether, the ethereal solution dried over calcium chloride, evaporated, and the residual oil fractionally distilled. Almost the whole quantity passed over between 230° and 255° as a colourless oil which solidified completely on cooling, and consisted of almost pure pyrocatechol. This method could no doubt be successfully carried out in digesters, and if the yield is as good as when hydriodic acid is used, pyrocatechol should be readily made at comparatively small cost.

Heriot Watt College,
Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

CONTRIBUTIONS FROM THE LABORATORIES OF THE HERIOT WATT COLLEGE, EDINBURGH.

Note on the Formation of Anthraquinone from Orthobenzoylbenzoic Acid.

By W. H. Perkin, Jun., Ph.D., F.R.S.

The constitution of anthraquinone and its derivatives has been proved by a number of elegant synthetical experiments, and, among these, the formation of monobromanthraquinone by the dehydrating action of sulphuric acid on orthobromorthobenzoylbenzoic acid (Pechmann, *Ber.*, **12**, 2127) is perhaps the most important—

$$C_6H_4Br\cdot CO\cdot C_6H_4\cdot COOH = C_6H_3Br<\begin{matrix}CO\\CO\end{matrix}>C_6H_4 + H_2O.$$

Liebermann (*Ber.*, **7**, 805) also showed that orthobenzoylbenzoic acid, when heated with fuming sulphuric acid, is converted into anthraquinonesulphonic acid; but no mention has been made of the formation of anthraquinone itself by the action of ordinary sulphuric acid on benzoylbenzoic acid, although it is well known that this change may be brought about by anhydrous phosphoric acid.

In the course of some experiments on benzoylbenzoic acid, I observed that this acid, in contact with ordinary sulphuric acid at 100°, is converted readily, and apparently quantitatively, into anthraquinone,

$$C_6H_5\cdot CO\cdot C_6H_4\cdot COOH = C_6H_4<\begin{matrix}CO\\CO\end{matrix}>C_6H_4 + H_2O.$$

The benzoylbenzoic acid employed in these experiments was prepared by acting on a mixture of phthalic anhydride and benzene with aluminium chloride (Pechmann, *Ber.*, **13**, 1612); it was repeatedly recrystallised from water, and thus obtained in long, thick needles, which, after drying at 115—120°, melted at 127°, and gave the following results on analysis :—

0·1420 gram substance gave 0·0568 gram H_2O and 0·3863 gram CO_2.

	Theory. $C_{14}H_{10}O_3$.	Found.
C	74·34 per cent.	74·19 per cent.
H	4·43 ,,	4·60 ,,
O	21·23 ,,	21·21 ,,

If this pure acid is dissolved in sulphuric acid, the yellow solu-

tion heated at 100° for half an hour, and the product poured into water, a white precipitate separates which consists for the most part of anthraquinone. The crude substance was collected, washed with water, digested with sodium hydrate solution to remove any unchanged acid, dried on a piece of porous plate, recrystallised from glacial acetic acid, and finally sublimed. In this way deep-yellow needles were obtained which melted at 275°, and consisted of pure anthraquinone.

This conversion of benzoylbenzoic acid into anthraquinone by means of sulphuric acid may be carried out well on the small scale as a lecture experiment. A small quantity of the finely divided acid is mixed in a test tube with sulphuric acid, the mixture heated at about 150° for a few seconds, and until the whole of the benzoylbenzoic acid has dissolved; the resulting deep-brown solution is then poured into water. If now an excess of sodium hydrate is added, the anthraquinone remains undissolved, and may be readily identified by warming with a little zinc-dust, when the well-known, characteristic, red-coloured liquid is obtained, which, if decanted and shaken with air, again deposits anthraquinone.

Heriot Watt College, Edinburgh.

HARRISON AND SONS, PRINTERS IN ORDINARY TO HER MAJESTY, ST. MARTIN'S LANE.

Author Perkin, William Henry and others 350688 C
Title Researches in organic chemistry. Vol.2 P4477re
DATE. NAME OF BORROWER.
May30 '30
University of Toronto Library
DO NOT REMOVE THE CARD FROM THIS POCKET
Acme Library Card Pocket
LOWE-MARTIN CO. LIMITED